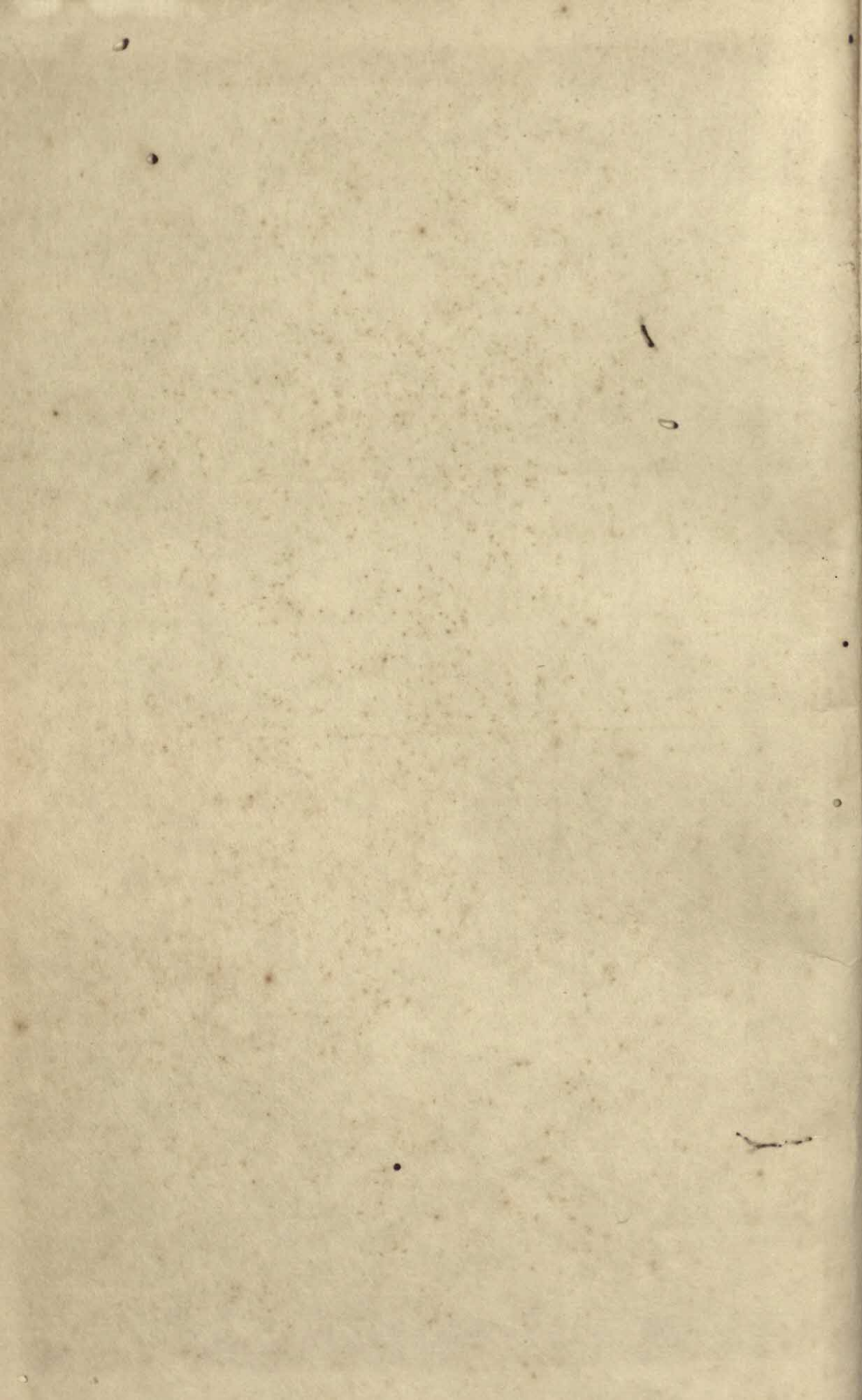


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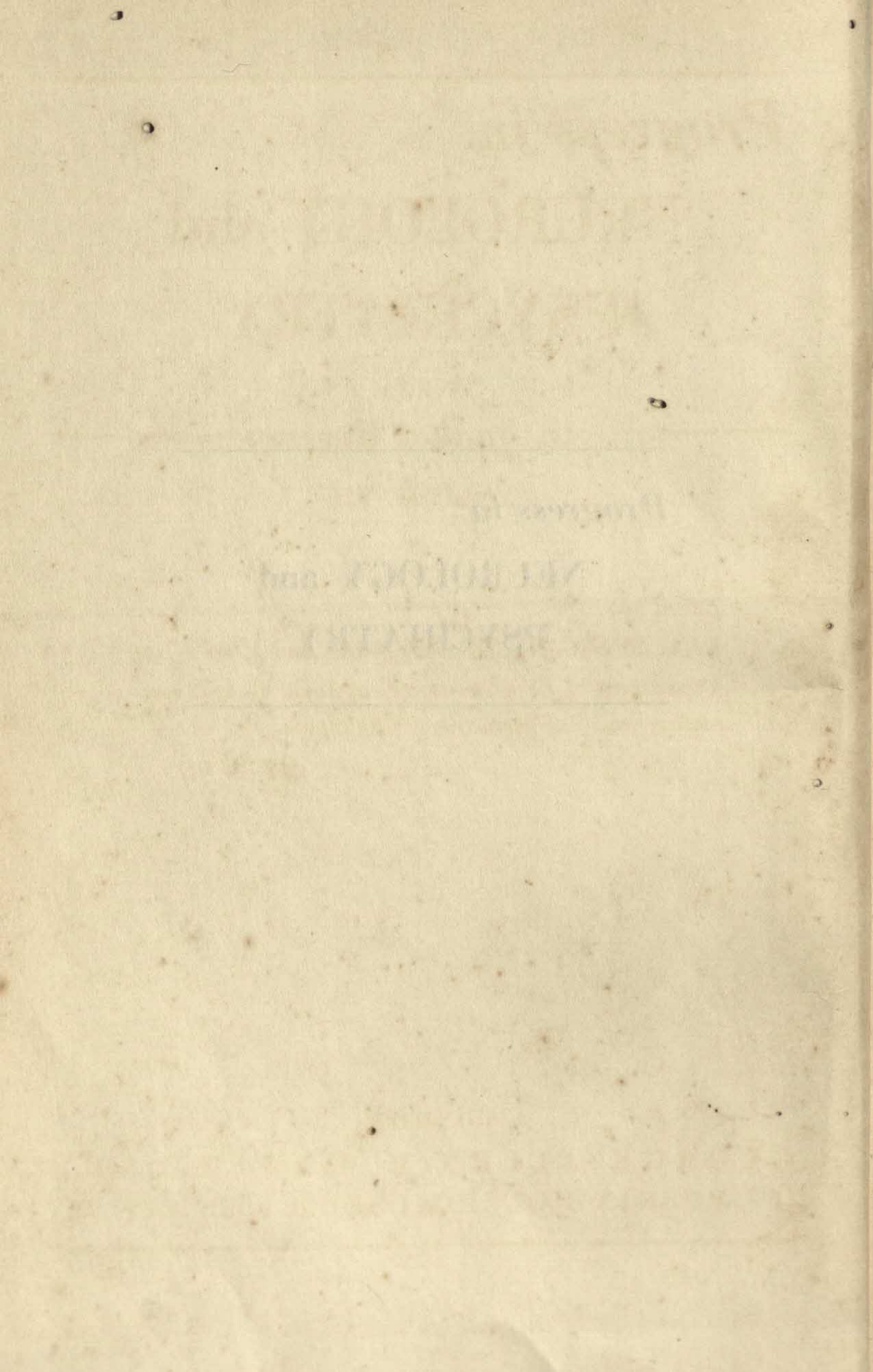
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Progress in

**NEUROLOGY and
PSYCHIATRY**



Progress in

**NEUROLOGY and
PSYCHIATRY**

An Annual Review

VOLUME VII

Edited by

E. A. SPIEGEL, M.D. *Professor and Head of the
Department of Experimental Neurology, Temple Uni-
versity School of Medicine, Philadelphia, Pa.*

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Preface

THERE is hardly a field of medicine in which the interrelationship between clinic and laboratory work is as obvious as in neurology and psychiatry. It may suffice to point out how far the therapy of infectious diseases of the nervous system has been influenced by the discovery of antibiotics, and how much the diagnosis of brain tumors has been facilitated by the introduction of radioactive substances. In the field of psychiatry, not only the understanding, but also further development, of electroshock treatment will ultimately depend on studies dealing with the effect of various types of currents upon the fundamental processes on which the excitation of the central nervous system depends. It seems, therefore, important that the readers of this series, although they are primarily clinically interested, should have an opportunity to become familiar with the advances of the basic disciplines as far as this is possible within the limits of this volume.

In the section dealing with Clinical Neurology, a new chapter on Pediatric Neurology has been included, and in the section on Clinical Psychiatry, a chapter on Genetics. For this latter chapter an internationally well known Swedish scientist and his associate have been invited in an attempt to further the international exchange of ideas by including non-American authors among the reviewers. Of the biennially reviewed subjects, this volume contains a chapter on Neurosyphilis in the section on Neurology and a chapter on Criminal Psychiatry in the section on Psychiatry.

It is the pleasant duty of the undersigned to express his sincere appreciation and deep gratitude to all reviewers who gave much of their valuable time for this project and particularly to Drs. M. Marks, H. T. Wycis and M. Kletzkin for helping in reading the proofs.

E. A. S.

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I. BASIC SCIENCES

CHAPTER 1

Neuro-Anatomy

By ELIZABETH C. CROSBY, Ph.D., Sc.D. AND RUSSELL T. WOODBURN, Ph.D.

GENERAL

THE interdependence of psychiatry and neuro-anatomy is generally recognized. The famous scholars, Cecile and Oskar Vogt,¹⁰¹ stressed the significance of neuro-anatomic data for psychiatry, and the great contributions of Adolf Meyer to neuro-anatomic fields have been emphasized by Rose.⁸² A philosophic discussion of the interrelation between the central nervous system and the periphery—and the role of each in the initiation of impulses—was presented by Holst.⁴⁷

The earlier development of the human nervous system was discussed by Streiter⁹² and Kahle.⁵⁴ Using several technics, including vital staining, Thomas⁹⁶ studied the nerve cells of various rodents to determine whether neurons could elaborate secretions. Barr and Bertram⁶ noted depletion from long periods of stimulation and then later restitution of Nissl substance in motor neurons. Bodian⁸ documented earlier observations that nodes of Ranvier occur within the central nervous system. Reissner's fiber was studied by Eberl-Rothe²⁹ in vertebrates from cyclostomes through primates. Observers (Onesti⁷³; John⁵², in cases of diencephalic rage; Clara,²² in relation to tuber cinereum and hypophysis) pointed out significant features of the barrier between the central nervous system and the vascular system or the meninges. Kautzky⁵⁵ thought that ontogenetic factors determine the specific cutaneous nerves over which stimuli from the meninges (or vessels) of the brain are referred to the periphery. In the walls of the cerebral ventricles, Friede^{34, 35} noted circumscribed sulcated areas (better developed in horse, cattle, and cat than in man) which appear early in ontogeny and which seem to have specific morphologic relations to certain brain nuclei. He believed that these released a substance into the ventricular fluid which had a bearing on sleep. Junker⁵³ found regressive

changes in the cells of the human cerebro-spinal fluid with the phase-contrast microscope.

New editions of the Larsell⁵⁹ and Buchanan¹⁶ texts on neuro-anatomy—both much improved in their present form—have appeared. The Villiger⁹⁹ atlas has been re-edited very satisfactorily by Rasmussen.

Erhart⁸¹ reported a simple, fast modification of the Pal-Weigert method for myelin sheaths. Einarson³⁰ employed certain dye-metal salts for quantitative estimation of basophilia in nerve cells and Bauer⁷ the shadowcasting technic of electron microscopy to show various structural relations in the central nervous system. By implanting radon seeds in the medulla, Borison and Wang¹³ produced well-circumscribed lesions, a method with many useful applications.

PERIPHERAL NERVES

Among the studies on peripheral nerves are those of Zander and Weddell¹¹⁰ and Peris⁷⁶ on the innervation of the cornea in various mammals. Livan and Del Bo⁶⁴ demonstrated previously undescribed nerve plexuses in the spiral lamina and along the internal spiral sulcus of man. Hermann⁴³ noted changes in neurons of the human nodose ganglion from birth to old age, and paraganglia were identified in this ganglion by Watzka and Scharf.¹⁰⁶ Williams^{107, 108} found afferent fibers to various laryngeal muscles in the internal laryngeal nerve. He regarded abductor paralysis as the result of muscle imbalance. Murtagh and Campbell⁷² believed that the laryngeal abductor muscle (in man, cat, and goat) is supplied by fibers of less than 2.8μ in diameter. DeVanna²⁸ documented the work of Huber and Guild on nervus terminalis in the rabbit.

Many observers have interested themselves in problems related to the autonomic nervous system. Hess⁴⁵ reviewed and supplemented his well known studies (see also McDonald⁶⁶) on the basic organization of the autonomic nervous system and the functional relations of various levels of the brain and spinal cord to it. Bradley¹⁴ described variations of surgical importance in the lower thoracic and lumbar sympathetic system. Hermann⁴⁴ studied various types of neurons in human sympathetic ganglia; both he and Hartig⁴² emphasized the binucleate character of some of these cells. Wrete¹⁰⁹ described numerous intermediate ganglia in the cervical rami communicantes of man. Rexed and von Euler⁷⁹ believed that histamine may be a specific constituent of certain unmyelinated fibers of the sympathetic nervous system. Using silver technics, Danon²⁷ studied signs of degeneration in the synapses in microganglia of the human adrenal gland. Boeke¹¹ reviewed his evidence for a terminal sympathetic "Grundplexus" as opposed to the terminal reticular net of Stöhr and others.

Lewy⁶¹ evaluated the evidence for the supposed role of the sphen-

palatine ganglion in some cases of head pain and concluded that the anatomic basis for such a role is insecure. In the rat, Lindsay⁶² traced part of the ocular postganglionic fibers through the tympanic cavity, a course demonstrated by others in several higher mammals including man. He regarded this course as due to embryologic relations of the postganglionic fibers to the stapedia artery. Mitchell⁷¹ studied the detailed innervation of the kidney in various mammals, including fetal and adult man. Lipp⁶³ described the innervation of the pulmonary valves of the heart in the guinea pig; Landau⁶⁸ that of the endocardium and the bundle of His in the calf; Field³³ the finer innervation of this bundle in a group of mammals; and Tcheng⁹⁵ the details of the synapses on the cardiac ganglia. In various mammals Magnenat⁶⁹ noted that the innervation of the alveoli, the respiratory bronchioles, and probably the alveolar capillaries of the lungs is by a sympathetic groundplexus. Kiss⁵⁶ found the adrenal medulla innervated chiefly by preganglionic fibers from the ventral roots of T7-9 and the adrenal cortex by postganglionics and sensory fibers from the spinal ganglia of T9-11. In the wall of the human gall bladder, Jabonero⁴⁸ described (a) ganglion cells which receive their major impulses from entering preganglionic neurons; (b) type I ganglion cells for intramural associations; and (c) a nervous syncytium with type II cells and (or) nerve fibers.

Sunderland and Bradley^{93, 94} studied the changes in the connective tissue and the amount of shrinkage of the endoneurial tubes in the distal stump of a severed nerve, and Cavanaugh¹⁷ the effect on the ganglion cells when the nerve is capped or crushed near the ganglion. The results of injury to corneal nerves (Zander and Weddell¹¹¹) and the problems of degeneration and regeneration in these nerves (Rexed and Rexed⁸⁰)—including regeneration in corneal grafts (rabbit, Rexed⁷⁸)—received considerable attention. Locatelli⁶⁵ showed the manner of degeneration and regeneration of nerves related to experimentally transplanted tumors.

BRAIN STEM AND SPINAL CORD

Romanes⁸¹ determined the various nuclear groups in the ventral horn gray of the lumbosacral cord in the cat and the relations of such groups or columns to the lumbosacral plexus and to the muscles they innervate. These columns presented a relatively definite pattern arrangement. On the contrary, Sprague⁹⁰ concluded, from his study of lumbar and thoracic levels of the macaque cord, that ventral horn cells cannot be classified functionally on the basis either of their topographic or morphologic relations. In the spider monkey, Chang¹⁸ described a caudal extension of Clarke's nucleus contributing fibers to the dorsal spino-cerebellar (Flechsig's) tract.

Angulo² found that the trigeminal ganglia in rat fetuses show considerably

earlier growth and differentiation than do the cervical ganglia. Walberg¹⁰² noted secondary subdivisions of the lateral reticular nucleus in various mammals, including man, and Brodal¹⁵ reported ascending fibers terminating, in somatotopic fashion, in this nucleus in the cat. He also traced spinal cord fibers to those circumscribed portions of the accessory olives which project to the anterior lobe of the cerebellum and to those portions of the inferior olive which connect with the pyramid and the uvula. He believed that fibers from all levels of the cord reach appropriate regions of the olive. Cranmer²⁶ presented an interesting series of diagrams and an interpretation of central vestibular and cerebello-vestibular interrelations based on anatomic as well as experimental and clinical data.³

The intraspinal course and the termination, in topographic fashion, of posterior root fibers within nucleus gracilis (or nucleus cuneatus) of the cat and the rabbit were studied by Glees, Livingston and Soler,³⁷ who believed that fasciculus cuneatus was formed only from roots of T₁ and cervical cord. Glees, Liddell and Phillips³⁶ showed that, in the cat's medulla, subolivary fibers of the medial lemniscus are intermingled with the fascicles of the pyramid. Matzke⁷⁰ studied the medial lemniscus in cats after destructive lesions involving nucleus gracilis and (or) nucleus cuneatus. His results agree essentially with those presented in previous studies of this system.

Schwartz, Roulhac, Lam and O'Leary⁸⁴ demonstrated the distribution of visceral afferent fibers of the 7th, 9th and 10th cranial nerves to fasciculus solitarius and its associated gray in man. It is valuable to have this pattern documented so clearly for the human brain.

CEREBELLUM

Jansen^{50, 51} gave a very interesting account of the development and adult anatomy of the cerebellum of whales, stressing its significant differences from that of man. The cerebellum of the whale has not only a rudimentary flocculo-nodular lobule, a greatly reduced hemisphere part of the anterior lobe, and a very small ansiform lobule, but also a markedly large lobulus simplex, an enormous paraflocculus, and a well developed paramedian lobule. Snider and Eldred⁸⁸ considered certain cerebro-cerebellar connections in the cat. This is a unit in the research program directed by the senior author on types of impulses relayed from various cord and brain centers to the cerebellum.

MIDBRAIN AND DIENCEPHALON

According to Warwick,¹⁰⁵ unilateral intracranial section of the oculomotor nerve produces degeneration in the ipsilateral oculomotor and the caudal $\frac{1}{3}$ of the contralateral oculomotor nucleus. In the cat, Reinoso

Saurez⁷⁷ described crossed and uncrossed medial and lateral rubrospinal systems; an ascending path appeared to reach zona incerta and the field of Forel, and another distributed to the ventral thalamic nucleus. The volume of various extrapyramidal centers (including red nucleus, substantia nigra, zona incerta, subthalamic nucleus, basal ganglia) was determined by von Bonin and Shariff¹² in a considerable range of mammals. They called attention to the marked reduction in the zona incerta in man and the increase in the putamen in primates.

In an interesting discussion of the functional anatomy of the thalamus, Rose⁸³ pointed out that experimentally defined areas of the dorsal thalamus project to specific architectonic fields of the cerebral cortex. Kuhlbeck⁵⁷ presented the nuclear topography and structure and the fiber connections of the human epithalamus and dorsal thalamus; his discussion of the functional and clinical significance of these areas is interesting. The cortical fields related to specific portions of the macaque pulvinar, as revealed by retrograde cell degeneration in this nucleus following small localized cortical lesions, have been pointed out by Chow.¹⁹ The results agree, in general, with those of other observers, but Chow's cortical fields are somewhat larger. Previous reports of transneuronal degeneration in the lateral geniculate nuclei of mammals, following destruction of one or both eyes, have been documented recently by Cook, Walker, and Barr²⁴ in cat and rabbit. The histologic changes occurring in retrograde and transneuronal degeneration have been well reviewed by Jacob.⁴⁹ Simma⁸⁵ demonstrated a connection of the parafascicular nucleus of the dorsal thalamus with the caudate and putamen at their region of fusion, and a projection of the mediodorsal part of centrum medianum to the head of the caudate nucleus, and its basolateral part to the putamen.

Hoff⁴⁶ discussed the anatomic relations, fiber connections, functions, and certain pathologic conditions of the hypothalamus. Auer⁸ noted the post-natal differentiation of the hypothalamic nuclei in the hamster, and Feremutsch³² the nuclear configuration of this region in man, where he found considerable variation from one brain to another. Green^{39, 40} gave a detailed account of the comparative anatomy of the hypophysis from *Amphioxus* to man. He also presented evidence against a rich innervation of the adenohypophysis. Among those who have considered the anatomy of hypothalamo-hypophyseal connections are Bodian⁹ (opossum), Bodian and Maren¹⁰ (rat), Spuler⁹¹ (guinea pig), Corona²⁵ (several mammals), Hagen⁴¹ (man), Christ²⁰ (man), and Orthner⁷⁴ (man). Evidence for the secretory functions of the supraoptic, paraventricular, and mammillo-infundibular nuclei has been presented by Smith⁸⁷ (rat), Ortmann⁷⁵ (rat; by showing restitution of the secretory substance after depletion), and others. Bargmann and Scharrer⁵ and Smith⁸⁷ have stressed the passage of

this secretion along the hypothalamo-hypophyseal tract with the neurohypophysis serving for storage. Spatz⁸⁹ documented the interrelations (nervous and vascular) between appropriate regions of the hypothalamus and the hypophysis. He regarded the supraoptico-hypophyseal tract as neurosecretory in function as well as serving for transportation of the secretion. Bodian⁹ stated that his studies on the hypophysis of the opossum tend to support the concept that the whole hypothalamo-hypophyseal system has secretory activity.

CEREBRAL HEMISPHERES

On the inner face of the dura, near the midline, at the junction of the cribriform plate with the frontal bone (rabbit, porpoise, 4 month human fetus), Sinclair⁸⁶ found a pair of ganglia. The functional connections of these ganglia are being studied.

A beautifully illustrated monograph by Conel²³ describing the cortical fields in the 6-month infant appeared this past year. LaVelle⁶⁰ studied the development of Nissl substance and nucleoli in the cortical neurones of fetal guinea pigs. Macchi⁶⁸ traced the embryologic development of the human rhinencephalon, emphasizing its specific organization as compared with that of corresponding areas in macromammals. Le Gros Clark²¹ discussed the pattern projected from the olfactory epithelium to the olfactory bulb in the adult rabbit.

From a study of silver impregnation material, Vaz Ferreira⁹⁷ gave a detailed analysis of cortical fields in the rat. Hemidecortication in this rodent (Vaz Ferreira and Combs⁹⁸) does not produce sufficient loss of interhemispheric connections to disturb markedly the characteristic patterns of cortical areas in the remaining hemisphere.

The published version of a recent lecture by Vogt¹⁰⁰ presents briefly, but very well, evidences of cortical localization from many sources. Bailey and von Bonin⁴ have written an excellent, comprehensive monograph on the human isocortex. It contains a consideration of the growth, weight, and fissuration of the brain and the general pattern of the isocortex; a detailed study, from serial sections, of the different cortical fields; and a discussion of the brain maps built up from the observations of various workers. It then describes intercortical association bundles and afferent and efferent cortical paths. It closes with a discussion of the functional significance of the isocortex.

A quite different approach to the problems of cortical localization has been taken by Walshe.¹⁰⁴ Although admitting the great additions to knowledge of brain function provided by the experimental method, he nevertheless felt that scientific thought has sometimes fared ill from the experimental approach. He objected particularly to the idea of a highly

specific pattern of functional localization within cortical fields. Walshe's paper is critical, argumentative at times, but stimulating. Gooddy and McKissock³⁸ suggested that the usefulness of the concept of strict cortical localization is past and would stress plasticity and compensation in brain functions. Such differences in point of view contribute greatly to a clarification of the interrelations of cortical structures and cortical functions.

Adey¹ demonstrated connections of the anterior cingulate gyrus and retrosplenial area with the presubiculum, the subiculum, the dentate gyrus, and the contralateral posterior cingulate and retrosplenial areas. In the monkey, Wall, Glees, and Fulton¹⁰³ traced cortico-fugal fibers from the posterior orbital cortex to the head of the caudate and to the paraventricular and ventromedial hypothalamic nuclei. McGrath⁶⁷ demonstrated, in the brain of a patient who succumbed 5½ years after a successful frontal lobe leucotomy, destruction of the anterior thalamic radiations, and major degeneration in the dorsomedial, and a minor involvement of the anterior, and anterior ventral, thalamic nuclei.

REFERENCES

- ¹ Adey, W. R.: An experimental study of the hippocampal connexions of the cingulate cortex in the rabbit. *Brain*. 74:233-247, 1951.
- ² Angulo, A. W.: A comparison of the growth and differentiation of the trigeminal ganglia with the cervical spinal ganglia in albino rat embryos. *J. Comp. Neurol.* 95:53-71, 1951.
- ³ Auer, J.: Postnatal cell differentiation in the hypothalamus of the hamster. *J. Comp. Neurol.* 95:17-41, 1951.
- ⁴ Bailey, P. and Bonin, G. v.: The isocortex of man. Illinois Monographs in the Medical Sciences. 6, nos. 1 & 2. Urbana, University of Illinois Press, 1951.
- ⁵ Bargmann, W. and Scharrer, E.: The site of origin of the hormones of the posterior pituitary. *Am. Scient.* 39:255-259, 1951.
- ⁶ Barr, M. L. and Bertram, E. G.: The behaviour of nuclear structures during depletion and restoration of Nissl material in motor neurons. *J. Anat.* 85:171-181, 1951.
- ⁷ Bauer, K. F.: Das Reliefbild des Nervengewebes. *Acta Anat.* 13:351-370, 1951.
- ⁸ Bodian, D.: A note on nodes of Ranvier in the central nervous system. *J. Comp. Neurol.* 94:475-483, 1951.
- ⁹ —: Nerve endings, neurosecretory substance and lobular organization of the neurohypophysis. *Bull. Johns Hopkins Hosp.* 89:354-376, 1951.
- ¹⁰ — and Maren, T. H.: The effect of neuro- and adeno-hypophysectomy on retrograde degeneration in hypothalamic nuclei of the rat. *J. Comp. Neurol.* 94:485-511, 1951.
- ¹¹ Boeke, J.: Sympathischer Grundplexus contra Terminalreticulum. *Acta Neuroveg.* 2:32-40, 1951.
- ¹² Bonin, G. v. and Shariff, G. A.: Extrapyramidal nuclei among mammals. A quantitative study. *J. Comp. Neurol.* 94:427-438, 1951.
- ¹³ Borison, H. L. and Wang, S. C.: Quantitative effects of radon implanted in the medulla oblongata: A technique for producing discrete lesions. *J. Comp. Neurol.* 94:33-55, 1951.

- ¹⁴ Bradley, K. C.: Observations on the surgical anatomy of the thoraco-lumbar sympathetic system. *Australian & New Zealand J. Surg.* 20:272-277, 1951.
- ¹⁵ Brodal, A.: Experimental studies on pathways from the spinal cord to the cerebellum. *Acta psychiat. et neurol. Suppl.* 74:83-84, 1951.
- ¹⁶ Buchanan, A. R.: *Functional Neuro-Anatomy*. Philadelphia, Lea & Febiger, 1951.
- ¹⁷ Cavanaugh, M.: Quantitative effects of the peripheral innervation area on nerves and spinal ganglion cells. *J. Comp. Neurol.* 94:181-219, 1951.
- ¹⁸ Chang, H.: Caudal extension of Clarke's nucleus in the spider monkey. *J. Comp. Neurol.* 95:43-51, 1951.
- ¹⁹ Chow, K. L.: A retrograde cell degeneration study of the cortical projection field of the pulvinar in the monkey. *J. Comp. Neurol.* 93:313-340, 1950.
- ²⁰ Christ, J.: Zur Anatomie des Tuber cinereum beim erwachsenen Menschen. (Mit besonderer Berücksichtigung der Beziehungen zur Hypophyse.) *Deutsche Ztschr. Nerven.* 165:340-408, 1951.
- ²¹ Clark, W. E. Le Gros: The projection of the olfactory epithelium on the olfactory bulb in the rabbit. *J. Neurol., Neurosurg. & Psychiat.* 14 (new series): 1-10, 1951.
- ²² Clara, M.: Zur Morphologie der Grenzsichten im nervösen Zentralorgan. *Deutsche Ztschr. Nerven.* 166:166-176, 1951.
- ²³ Conel, J. L.: The Postnatal Development of the Human Cerebral Cortex. Vol. IV, The cortex of the six-month infant. Cambridge, Harvard University Press, 1951.
- ²⁴ Cook, W. H., Walker, J. H., and Barr, M. L.: A cytological study of transneuronal atrophy in the cat and the rabbit. *J. Comp. Neurol.* 94:267-291, 1951.
- ²⁵ Corona, G. L.: Contributo alla conoscenza della struttura e della innervazione della neuroipofisi. *Ztschr. Anat. u. Entwicklungsgesch.* 115:658-675, 1951.
- ²⁶ Cranmer, R.: Nystagmus related to lesions of the central vestibular apparatus and the cerebellum. *Ann. Otol., Rhin. & Laryng.* 60:186-196, 1951.
- ²⁷ Danon, D.: Variations de la structure des synapses dans les ganglions sympathiques chez l'homme. *Acta Anat.* 13:163-170, 1951.
- ²⁸ DeVanna, F.: Distribuzione periferica del nervo terminale e suo cellule nei mammiferi. *Arch. ital. anat. e. embriol.* 56:1-20, 1951.
- ²⁹ Eberl-Rothe, G.: Über den Reissnerschen Faden der Wirbeltiere. *Ztschr. f. mikr.-anat. Forschung.* 57:137-180, 1951.
- ³⁰ Einarson, L.: On basophilia of nerve cells and its quantitative estimation by staining with inner complex dye-metal salts. *Acta psychiat. et neurol. Suppl.* 74:85-87, 1951.
- ³¹ Erhart, E. A.: A simple, fast, controllable modification of Pal-Weigerts' stain for myelin sheaths. *Ztschr. wissen. mikr. u. mikr. tech.* 6:155-156, 1951.
- ³² Feremutsch, K.: Die Variabilität der cytoarchitektonischen Struktur des menschlichen Hypothalamus. *Monatschr. f. Psychiat. u. Neurol.* 121:87-113, 1951.
- ³³ Field, E. J.: The nervous component of the atrioventricular bundle. *J. Anat.* 85:105-112, 1951.
- ³⁴ Friede, R.: Über Furchenfelder in den Wandungen der Hirnventrikel. *Acta Neuroveg.* 2:84-97, 1951.
- ³⁵ —: Über zentral-humorale Schlafsteuerung. *Acta Neuroveg.* 2:270-283, 1951.
- ³⁶ Glees, P., Liddell, E. G. T., and Phillips, C. G.: Der Verlauf der medialen Schleife im Hirnstamm der Katze. *Ztschr. Zellforsch. u. mikr. Anat.* 35:487-494, 1951.

- ³⁷ Glees, P., Livingston, R. B., and Soler, J.: Der intraspinale Verlauf und die Endigungen der sensorischen Wurzeln in den Nucleus Gracilis und Cuneatus. *Ztschr. ges. Neurol. u. Psychiat.* 187:190-204, 1951.
- ³⁸ Gooddy, W., and McKissock, W.: The theory of cerebral localization. *Lancet.* 260:481-483, 1951.
- ³⁹ Green, J. D.: The comparative anatomy of the hypophysis, with special reference to its blood supply and innervation. *Am. J. Anat.* 88:225-311, 1951.
- ⁴⁰ —: Innervation of the pars distalis of the adenohipophysis studied by phase microscopy. *Anat. Rec.* 109:99-107, 1951.
- ⁴¹ Hagen, E.: Neurohistologische Beobachtungen an Hypophyse und Zwischenhirn des Menschen. *Acta Neuroveg.* 3:67-76, 1951.
- ⁴² Hartig, K.: Zâr Frage der Zweikernigkeit sympathischer Ganglienzellen III. *Ztschr. Zellforsch. u. mikr. Anat.* 36:268-272, 1951.
- ⁴³ Hermann, H.: Mikroskopische Studien über Alterveränderungen am Ganglion nodosum N. vagi des Menschen. *Ztschr. Zellforsch. u. mikr. Anat.* 36:151-170, 1951.
- ⁴⁴ —: Mikroskopische Studien am Grenzstrang des Sympathikus beim Menschen. *Anat. Anz.* 98:181-185, 1951.
- ⁴⁵ Hess, W. R.: Prinzipien organischer Ordnung am Beispiel des vegetativen Nervensystems. *Klin. Wchnschr.* 29:105-111, 1951.
- ⁴⁶ Hoff, H.: Die Pathologie des Hypothalamus. *Wien klin. Wchnschr.* 63:57-62, 1951.
- ⁴⁷ Holst, E. V.: Zentralnervensystem und Peripherie in ihrem gegenseitigen Verhältnis. *Klin. Wchnschr.* 29:97-105, 1951.
- ⁴⁸ Jabonero, V.: Études sur le système neurovégétatif périphérique. IV. Innervation intramurale de la vesicule biliaire humaine. *Acta Anat.* 13:171-192, 1951.
- ⁴⁹ Jacob, H.: Zur Histopathologie der retrograden und transneuronalen Degeneration. *Deutsche Ztschr. Nerven.* 166:146-165, 1951.
- ⁵⁰ Jansen, J.: The morphogenesis of the cetacean cerebellum. *J. Comp. Neurol.* 93:341-400, 1950.
- ⁵¹ —: The cerebellum of man in the light of studies of the cerebellum of whales. *Acta psychiat. et neurol. Suppl.* 74:80-82, 1951.
- ⁵² John, E.: Schädel-Hirntrauma, vegetatives Nervensystem und Ausnahmezustände. *Acta Neuroveg.* 2:163-170, 1951.
- ⁵³ Junker, F.: Die Zellen des Liquor cerebrospinalis im Phasenkontrastmikroskop. *Deutsche Ztschr. Nerven.* 166:237-246, 1951.
- ⁵⁴ Kahle, W.: Studien über die Matrixphasen und die örtlichen Reifungsunterschiede im embryonalen menschlichen Gehirn. 1. Mitteilung. Die Matrixphasen im allgemeinen. *Deutsche Ztschr. Nerven.* 166:273-302, 1951.
- ⁵⁵ Kautzky, R.: Ein Grundplan der cerebrospinalen Innervation der Hirnhäute und Hirngefäße. *Ztschr. Anat. u. Entwicklungsgesch.* 115:570-583, 1951.
- ⁵⁶ Kiss, T.: Experimentell-morphologische Analyse der Nebenniereninnervation. *Acta Anat.* 13:81-89, 1951.
- ⁵⁷ Kuhlbeck, H.: The derivatives of thalamus dorsalis and epithalamus in the human brain: Their relation to cortical and other centers. *Mil. Surgeon.* 108:205-256, 1951.
- ⁵⁸ Landau, E.: III. Contribution à l'innervation du coeur (fibres myélinisées). *Acta Anat.* 13:119-124, 1951.

- ⁵⁹ Larsell, O.: *Anatomy of the Nervous System*. New York, Appleton-Century-Crofts, Inc., 1951.
- ⁶⁰ LaVelle, A.: Nucleolar changes and development of Nissl substance in the cerebral cortex of fetal guinea pigs. *J. Comp. Neurol.* 94:453-473, 1951.
- ⁶¹ Lewy, R. B.: Anatomical and clinical evaluation of head pain attributed to the sphenopalatine ganglion. *J. Laryng. & Otol.* 65:10-13, 1951.
- ⁶² Lindsay, J. S. B.: The association of ocular sympathetic pathways with the stapedial artery in the albino rat. *J. Comp. Neurol.* 94:371-379, 1951.
- ⁶³ Lipp, W.: Studien zur Herzinnervation. I. Die Innervation der Pulmonalisklappen. *Acta Anat.* 13:30-62, 1951.
- ⁶⁴ Livan, M. and Del Bo, M.: De l'existence d'un plexus nerveux marginal et paramarginal au niveau de la lame spirale et du sillon spiral interne chez l'homme. *Acta Anat.* 13:16-29, 1951.
- ⁶⁵ Locatelli, P.: Sulla rigenerazione delle fibre nervose durante lo sviluppo di tumori sperimentali. *Arch. sc. med.* 91:461-477, 1951.
- ⁶⁶ McDonald, D. A.: W. R. Hess: The control of the autonomic nervous system by the hypothalamus. *Lancet.* 260:627-629, 1951.
- ⁶⁷ McGrath, S. D.: Clinico-anatomical study of a successful leucotomy. *Lancet.* 260:385-387, 1951.
- ⁶⁸ Macchi, G.: The ontogenetic development of the olfactory telencephalon in man. *J. Comp. Neurol.* 95:245-305, 1951.
- ⁶⁹ Magnenat, P.: Étude neurohistologique du poumon. *Acta Anat.* 13:193-224, 1951.
- ⁷⁰ Matzke, H. A.: The course of the fibers arising from the nucleus gracilis and cuneatus of the cat. *J. Comp. Neurol.* 94:439-452, 1951.
- ⁷¹ Mitchell, G. A. G.: The intrinsic renal nerves. *Acta Anat.* 13:1-15, 1951.
- ⁷² Murtagh, J. A. and Campbell, C. J.: The respiratory function of the larynx. III—The relation of fibre size to function in the recurrent laryngeal nerve. *Laryngoscope.* 61:581-590, 1951.
- ⁷³ Onesti, S. J.: The blood-brain barrier. *McGill M. J.* 19:203-210, 1951.
- ⁷⁴ Orthner, H.: Anatomische Befunde im Hypophysen-Hypothalamus-System bei Fehlen der intrasellären Hypophyse und bei Kastration. *Acta Neuroveg.* 3:50-53, 1951.
- ⁷⁵ Ortmann, R.: Über experimentelle Veränderungen der Morphologie des Hypophysen Zwischenhirnsystems und die Beziehung der sog. "Gomorisubstanz" zum Adiuretin. *Ztschr. Zellforsch. u. mikr. Anat.* 36:92-140, 1951.
- ⁷⁶ Peris, E. F.: Le problème de l'innervation de la cornée. *Acta Anat.* 13:63-80, 1951.
- ⁷⁷ Reinoso Saurez, F.: Aportaciones a la sistematización rubrifuga. *Actual. méd. Granada.* 27:94-98, 1951. (Quoted from *Excerpta med.* 6:22, 1952.)
- ⁷⁸ Rexed, U.: Nerve regeneration in corneal grafts in the rabbit. *Brit. J. Ophth.* 35:89-97, 1951.
- ⁷⁹ Rexed, B. and Euler, U. S. v.: The presence of histamine and noradrenaline in nerves as related to their content of myelinated and unmyelinated fibers. *Acta psychiat. et neurol.* 26:61-65, 1951.
- ⁸⁰ Rexed, B. and Rexed, U.: Degeneration and regeneration of corneal nerves. *Brit. J. Ophth.* 35:38-49, 1951.
- ⁸¹ Romanes, G. L.: The motor cell columns of the lumbo-sacral spinal cord of the cat. *J. Comp. Neurol.* 94:313-363, 1951.

- ⁸² Rose, J. E.: Adolph Meyer's contributions to neuro-anatomy. *Bull. Johns Hopkins Hosp. Suppl.* 89:56-59, 1951.
- ⁸³ —: Some modern aspects of the functional anatomy of the thalamus. *Monatschr. f. Psychiat. u. Neurol.* 120:378-387, 1950.
- ⁸⁴ Schwartz, H. G., Roulhac, G. E., Lam, R. L., and O'Leary, J. L.: Organization of the fasciculus solitarius in man. *J. Comp. Neurol.* 94:221-237, 1951.
- ⁸⁵ Simma, K.: Zur Projektion des Centrum medianum und Nucleus parafascicularis thalami beim Menschen. *Monatschr. f. Psychiat. u. Neurol.* 122:32-46, 1951.
- ⁸⁶ Sinclair, J. G.: A ganglionic plexus in the human falx cerebri. *Texas Rep. Biol. & Med.* 9:348-352, 1951.
- ⁸⁷ Smith, S. W.: The correspondence between hypothalamic neurosecretory material and neurohypophyseal material in vertebrates. *Am. J. Anat.* 89:195-231, 1951.
- ⁸⁸ Snider, R. and Eldred, E.: Electro-anatomical studies on cerebro-cerebellar connections in the cat. *J. Comp. Neurol.* 95:1-16, 1951.
- ⁸⁹ Spatz, H.: Neues über die Verknüpfung von Hypophyse und Hypothalamus. *Acta Neuroveg.* 3:5-49, 1951.
- ⁹⁰ Sprague, J. M.: Motor and propriospinal cells in the thoracic and lumbar ventral horn of the rhesus monkey. *J. Comp. Neurol.* 95:103-123, 1951.
- ⁹¹ Spuler, H.: Über das Tuber cinereum des Meerschweinchens und seine topographischen Beziehungen zum Infundibulum. *Acta Anat.* 13:125-162, 1951.
- ⁹² Streiter, A.: Ein menschlicher Keimling mit 7 Urvirbelpaaren. (Keimling Ludwig) *Ztschr. f. mikr.-anat. Forschung.* 57:181-248, 1951.
- ⁹³ Sunderland, S. and Bradley, K. C.: Denervation atrophy of the distal stump of a severed nerve. *J. Comp. Neurol.* 93:401-409, 1950.
- ⁹⁴ —: Endoneurial tube shrinkage in the distal segment of a severed nerve. *J. Comp. Neurol.* 93:411-420, 1950.
- ⁹⁵ Tcheng, K. T.: Synapses interneuronales dans les ganglions cardiaques. *Acta Anat.* 11:431-443, 1951.
- ⁹⁶ Thomas, O. L.: A comparative study of the cytology of the nerve cell with reference to the problem of neurosecretion. *J. Comp. Neurol.* 95:73-99, 1951.
- ⁹⁷ Vaz Ferreira, A.: The cortical areas of the albino rat studied by silver impregnation. *J. Comp. Neurol.* 95:177-243, 1951.
- ⁹⁸ — and Combs, C. M.: Structure of the cortical areas after hemidecortication in the albino rat. *Acta Anat.* 13:225-231, 1951.
- ⁹⁹ Villiger, E.: Atlas of Cross-Section Anatomy of the Brain. 14th edition reviewed by Ludwig, E.; Rasmussen, A. T. (ed): Philadelphia, Blakiston Co., 1951.
- ¹⁰⁰ Vogt, O.: Die anatomische Vertiefung der menschlichen Hirnlokalisation. *Klin. Wehnschr.* 29:111-125, 1951.
- ¹⁰¹ Vogt, C. and Vogt, O.: Importance of neuroanatomy in the field of neuropathology. *Neurology.* 1:205-218, 1951.
- ¹⁰² Walberg, F.: The lateral reticular nucleus of the medulla oblongata. A comparative-anatomical study. *Acta psychiat. et neurol., Suppl.* 74:92-94, 1951.
- ¹⁰³ Wall, P. D., Gleses, P., and Fulton, J. F.: Corticofugal connections of posterior orbital surface in rhesus monkey. *Brain.* 74:66-71, 1951.
- ¹⁰⁴ Walshe, F. M. R.: On the interpretation of experimental studies of cortical motor function: With special reference to the "operational view" of experimental procedures. *Brain.* 74:249-266, 1951.
- ¹⁰⁵ Warwick, R.: A study of retrograde degeneration in the oculomotor nucleus of

- the rhesus monkey, with a note on a method of recording its distribution. *Brain*. 73:532-541, 1950.
- ¹⁰⁶ Watzka, M. and Scharf, J. H.: Die Paraganglien am Ganglion nodosum vagi und dessen Umgebung beim erwachsenen Menschen. *Ztschr. Zellforsch. u. mikr. Anat.* 36:141-150, 1951.
- ¹⁰⁷ Williams, A. F.: The nerve supply of the laryngeal muscles. *J. Laryng. & Otol.* 65:343-348, 1951.
- ¹⁰⁸ —: Observations on abductor paralysis of the vocal cords. *J. Laryng. & Otol.* 65:397-403, 1951.
- ¹⁰⁹ Wrege, M.: Ganglia of rami communicantes in man and mammals particularly monkey. *Acta Anat.* 13:329-336, 1951.
- ¹¹⁰ Zander, E. and Weddell, G.: Observations on the innervation of the cornea. *J. Anat.* 85:68-99, 1951.
- ¹¹¹ —: Reaction of corneal nerve fibers to injury. *Brit. J. Ophth.* 35:61-88, 1951.

General Neurophysiology

By HARRY GRUNDFEST, Ph.D.

GENERAL SURVEY

Reviews and Books

UNDOUBTEDLY the most important review published in the past year is Hodgkin's *The Ionic Basis of Electrical Activity in Nerve and Muscle*.¹³⁰ The Woods Hole volume of lectures in memory of Leonor Michaelis, edited by Barron,²⁵ contains a number of chapters on neurophysiology. Sections on the red cell membrane²⁰⁴ and permeability¹⁴⁰ will yield valuable information on a topic related to that of nerve. For special treatments of the problems of neurophysiology, there are chapters by Steinbach,²⁴⁵ Grundfest,¹¹⁴ Nachmansohn,¹⁹⁵ Kuffler,¹⁵³ Tobias²⁶⁵ and Prosser.²⁰⁸

The second Josiah Macy, Jr. Conference on Nerve Impulse¹⁹⁴ contains an informal presentation of special fields of neurophysiology by Steinbach,²⁴³ Bishop,³⁰ Brooks and Fuortes,³⁹ Brink³⁵ and Folch-Pi.⁹² As was true for the First Conference,¹⁹³ the interspersed comments and discussions by the heterogenous group of participants are often illuminating and offer new ideas regarding the many unsolved problems in the field.*

Two reviews present the energetic¹⁹⁶ and enzymatic¹⁹⁷ aspects of neurochemical activity. Shanes²³⁴ has summarized the results of his work on ionic and metabolic factors in nerve functioning. Young's review of characteristics of nerve fibers²⁹⁵ should also prove useful to the neurophysiologist. Extensive summaries of three important papers by Conway,⁶⁰ Hodgkin¹²⁹ and Ussing,²⁶⁸ presented at the 18th International Physiological Congress as parts of a symposium on ion movements, have been mimeographed and distributed by the Office of Naval Research. Eccles⁷⁸ has reviewed the problem of the origin of cortical potentials, as has Wyss.²⁸⁷

Attention is called to the *Colloque International d'Électrophysiologie*, which was held in 1949. The papers published as Nos. 2, 3, and 4 of Volume III of the Arch. Sci. Physiol. of that year were not issued, however,

* The Handbook of Experimental Psychology (S. Stevens, ed., New York, Wiley, 1951), has two chapters by F. Brink, Jr., on neurophysiology, and much additional neurophysiologic information is to be found in other chapters.

until late in 1950. The Annual Review of Physiology for 1951 had two sections of major interest to neurophysiologists; one by Steinbach on permeability²⁴⁴ and the other by Bullock on conduction and transmission of nerve impulses.⁴¹ Volume I of *Progress in Biophysics* has a valuable discussion of bioelectric potentials by Crane.⁶⁴

The cooperative textbook, *Comparative Animal Physiology*, edited by Prosser,²⁰⁷ contains several chapters useful to the student of neurophysiology, as does Davson's *Text Book on General Physiology*,⁶⁷ written by an expert in permeability aspects of cell physiology. A small textbook on electroneurophysiology by Brazier,³⁵ is intended for beginners in the field and in extremely compressed form presents the general field well. The reviewer also desires to call attention to a small book, *Electrophysiological Technique*,⁷¹ which was published in England in 1950.

New Work

Essentially, the past year has been one of consolidation of earlier developments. An important series of papers by Keynes, some with his colleague Lewis,¹⁴⁶⁻¹⁴⁸ detail quantitatively the ion movements in nerve fibers during rest and activity. By an ingenious method, Huxley and Stämpfli¹³⁷⁻¹³⁹ have demonstrated overshoot in single myelinated fibers and the relation between spike height and sodium concentration. They have also measured the resting potential as well as its modification by external ion changes. Weidman²⁷⁷⁻²⁷⁹ has used the glass microelectrode for measurement of the characteristics of single squid axons and Purkinje fibers. Draper and Weidman⁷³ have demonstrated overshoot in mammalian Purkinje fibers, and Woodbury et al.,²⁸⁵ in frog ventricle. An important paper by Fatt and Katz²⁴ presents a wealth of data of the motor end plate, and Nastuk^{198, 199} in preliminary papers, describes some parallel findings.

Exciting work by Eccles and his colleagues is as yet only available in a preliminary report³⁶ and in the unpublished 1951 Adam Miller Lecture on microelectrode recording from the interior of single motoneurons in the mammal. The resting potential is about 90 mv, the spike shows an overshoot, has a duration of about 1 msec, and is followed by negative and positive after potentials of the same form, but of larger magnitude than those found in mammalian A fibers.

Rushton²²² has extended his treatment of the excitable properties of nerve fibers. Tasaki²⁵⁶⁻²⁶¹ has further developed his theory of excitation supported with good experimental data. Saltatory conduction appears to have become more firmly established by new anatomic data³¹ and by neurophysiological experiments.

The sometimes acrimonious discussion on the sheath as a barrier to ion movements seems to have been settled by new work of Feng and Liu,⁸⁷

Crescitelli⁸⁵ and Lundberg¹⁸³ although alternative explanations for some of the data are presented by Lorente de N6.¹⁷⁶⁻¹⁷⁸

Fatt⁸³ and Fatt and Katz⁸⁴ have presented interesting data on the pharmacology of vertebrate and invertebrate neuromuscular junctions. The reviewer and his colleagues have demonstrated the blocking action of curare and the inactivators of acetylcholinesterases as well as of acetylcholine in squid giant axon,¹¹⁸ by microinjection of minute quantities of these substances. Monnier and his group^{191, 192} have extended their studies on the "damping" phenomenon.

Arvanitaki and Chalazonitis have continued work on the metabolic elements of the axon and nerve cell.^{18, 20, 52} Chagas and his colleagues⁵¹ have developed a useful slice preparation for study of the electric eel and with the Fessards and Albe-Fessard, particularly,⁴⁻¹⁰ have been extending their experimental studies on the physical and physiologic behavior of the electroplax. Grundfest, Nachmansohn and their colleagues have recently undertaken similar studies with important new observations reported in a preliminary note.^{11*} Bullock,⁴²⁻⁴⁵ Wiersma²⁸¹⁻²⁸³ and others have introduced new invertebrate axonal and synaptic preparations and have presented new electrophysiologic data particularly on peripheral integrating mechanisms. From Kuffler^{134, 135, 156} has come the full account of the control mechanism which is constituted by the small motor fiber system of mammals.

A number of papers, particularly from Zotterman's laboratory^{13, 14, 121-126} and by Gray et al.¹⁰⁴⁻¹⁰⁸ have produced new information on the behavior and properties of several types of sensory receptors.

New Developments in Technic

The glass (Ling) microelectrode technic as improved by Hodgkin and his colleagues²⁰⁰ for recording action potentials has become widely used and is furnishing extremely valuable results. Particularly noteworthy is the demonstration^{73, 277-279} that the microelectrode can be repeatedly inserted into a nerve or Purkinje fiber apparently without excessive damage to its properties or function. The use by Eccles and his colleagues of microelectrodes in the technically much more difficult situation of the spinal cord has already been mentioned.³⁶ In the hands of Katz and Fatt,⁸⁴ the microelectrode technic has proved its value towards important data in the myoneural junction and muscle fibers. Svaetichin²⁵² has described a new type of glass and metal microelectrode. The lumen of the capillary is filled with silver and the tip is then plated with rhodium and platinum

* R. D. Keynes and H. Martins-Ferreira (J. Physiol., 116, 1952) have reported independent and earlier work on resting and action potentials in the single units of the electric organ.

black. These electrodes have low resistance and good DC stability. They are also suitable for measurements at high frequencies.¹⁰⁹ The same author has also described an elaborate apparatus for study of single cells.²⁵³ An interesting paper on the results of his studies with frog and cat spinal ganglion cells²⁵⁴ will be referred to later.

Huxley and Stämpfli's¹³⁷⁻¹³⁹ ingenious circuit analysis has formulated a method which permits them to measure by external electrodes the resting and action potentials of frog single myelinated nerve fibers. The method depends on so arranging the circuit elements external to the nerve fiber as to be able to balance the potentials to be measured by applied pulses of known voltage.

Keynes and Lewis¹⁴⁸ have employed "activation analysis," as will be described later, to measure ionic concentration in axons. Their precise technical and analytic use of standard tracer technics should also be signalized.

Of prime importance is the method developed by Hodgkin, Huxley and Katz^{131b} to analyze the sequence of ion changes during activity. This method is an adaptation of that used by Cole and Marmont¹⁸⁹ for recording membrane voltage with relatively zero membrane current flow. In the form used by Hodgkin, Huxley and Katz, a pair of internal electrodes sense and maintain by feedback zero voltage difference across a region of the excitable membrane of the giant axon. The capacitative current flow then vanishes and the ionic flow is measurable. The time course of the current flow is determined for a number of voltage values of the membrane so "clamped" against other regions of the membrane which are allowed to undergo their normal behavior. By measuring the magnitude, direction and time course of the current change with external solutions of various compositions, Hodgkin, Huxley and Katz have been able to deduce, in main outline, the component ions which participate in carrying the current during the course of activity.¹³⁰

THE PHYSICAL AND PHYSICO-CHEMICAL PROPERTIES OF THE BIOELECTRIC GENERATOR

The Physical Properties of Nerve and Their Changes in Activity

The work of Hill on the optical and physical changes which occur in nerve^{127, 128} and parallel work by Tobias and his colleagues (as summarized²⁶⁵), demonstrates that a complex series of physical changes takes place in active nerve. However, only a small proportion of giant axons were observed to show turgidity on stimulation.⁶³ The same author observed no dimensional changes on activity. A piezo-electric, or electrostrictive mechanism for the bioelectric potential is suggested.⁹⁵ At the moment, it

is not possible to relate these various physical changes directly to the activity, because the methods are still relatively too insensitive (though their absolute sensitivity is extraordinarily high), and accordingly depend upon measurement of relatively slow changes in response to repetitive stimulation. Therefore, it is not known which, if any, of these changes are a prelude to the spike and which are consequent to the ionic changes of the activity.

The axoplasm of the giant axon is said to be in the gel state as demonstrated by microinjection technics.⁵³ Oil or air injected into the center of the axon assumes an oval shape. Toward the periphery the bubbles are narrow cylinders, indicating a longitudinal structural arrangement. The axoplasmic gel is liquified by excess of Ca. Ingenious experiments by Hodgkin and Keynes¹³² using tracer technic, indicates that the internal potassium of the giant axon exists largely as the free ions, with mobility as in sea water.

Electrical Circuit Properties

Lussier and Rushton¹⁸⁶ have contributed a valuable experimental study of the space constant in frog A fibers. This constant is smaller for the fibers of smaller diameter and is proportional to conduction velocity. Its experimental value is also a function of duration of the stimulus used to determine the constant. A masterly attempt by Rushton²²² to relate various aspects of the behavior of medullated nerve fibers to consequences derived from cable theory has produced some valuable insight into this problem. Of very great interest to the reviewer was Rushton's interpretation of the significance of the ratio between the axonal diameter and the total diameter of the myelinated fiber, as well as the correlation with cable theory of the experimentally observed relations between thresholds, spike duration, refractory period, chronaxie and summation time and fiber diameter. Two serious discrepancies have been found, however. The spike height is proportional to fiber diameter,¹⁰⁰ whereas Rushton points out that his derivation would predict a proportionality to D^2 . Rushton finds that the theory agrees with experiments in that the conduction velocity of myelinated fibers should be also proportional to D .¹³⁶ Nevertheless, for unmyelinated fibers the prediction is of proportionality to $\sqrt{D}$. This relation has been found by Pumphrey and Young²¹¹ for invertebrate nerves, but not by Gasser⁹⁹ for vertebrate C fibers. The discrepancy is still worse if Pumphrey and Young's data are reexamined (personal communication from R. Hodes). The $\sqrt{D}$ relation was obtained by including measurements of small nerve fibers with those on giant axons, a procedure which assumes that the proportionality constant is the same for both kinds of nerve fibers. Hodes finds, however, that if only one kind of fiber is studied (giant axons of

squid *in situ*) the relation between conduction velocity and diameter is nearly linear, as it is in vertebrate nerve fibers.

Adey,² furthermore, reports that in the giant axons of the earthworm (*Megascolex*) the conduction velocity (as high as 30–40 m/sec) is also directly proportional to the fiber diameter, and that there is a similar proportionality to the length of the animal. Thus, Rushton's excellent treatment falls down on two counts. It does not predict correctly the potential recorded from fibers of different diameters (observed proportional to D ; theory proportional to D^2) and it predicts that for unmyelinated nerve fibers the velocity should be proportional to $\sqrt{D}$.

This writer believes that the failure is caused by neglect of an invariant term—the observed constancy of the spike duration. He is sympathetic to Hodgkin's¹³⁰ suggestion that the low measured capacity of the myelinated nerve fiber is a function of the capacities of the myelin lamellae in series with the capacity of the membrane. The overall capacity would then be relatively insensitive to changes in the number of lamellae if these change for fibers of different diameters. If the spike duration is roughly a function of the RC product, this latter must, therefore, be a constant. Now, R is the entire series circuit resistance of the membrane, the external current path and the internal path. The latter must vary with the diameter of the fiber, increasing for the smaller fibers. From the invariant spike duration and the relatively invariant capacity, it then follows that total R must also depend on the diameter in such a way as to remain essentially constant. Gasser and Grundfest¹⁰⁰ used the variation of the wavelength with fiber diameter inductively to derive the proportionality of the recorded spike height to the fiber diameter.

Opatowsky²⁰² has taken into account the constancy of the spike duration. But his formal derivation of the conduction velocity "does not make use of any other field of science beyond the fundamental principles of electricity." It employs an inductance in the equivalent circuit, which as the writer has indicated elsewhere in this review, is analogical reasoning carried too far.

The reviewer would like to emphasize that the classical distinction (such as Rushton uses) of "myelinated" and "unmyelinated" nerve fibers, while it has undoubted reality for certain phenomena—as in the demonstration of saltatory conduction—may not be as useful a concept in other cases. "Unmyelinated" nerve fibers are so only by virtue of nomenclature. For vertebrate "unmyelinated" fibers the limitations of size have prevented accurate observation, but in the giant axon of squid a thin myelin sheath is easily observed. The barrier for the quaternary ammonium salts to penetration of the excitable membrane in certain tissues but not in others also needs to be explained. Nachmansohn at one time tended to correlate

this barrier with the myelin sheath. Yet, this barrier is present also in "unmyelinated" nerve fibers, vertebrate as well as invertebrate, and in muscle fibers. The existence of the barrier, which is absent at end plates and other junctions, indicates that some form of "myelin" covering is present in all longitudinally extensive cellular structures, and its presence will need to be taken into account in cable circuit theory.

Further studies on the electrical constants of excitable tissues and of their dynamic properties have been carried out by Draper and Weidmann,⁷³ and Fatt and Katz.⁸⁴ Weidmann²⁷⁷ has used the glass microelectrode to redetermine the characteristic of giant axons with results essentially those obtained by other methods. He found rather low leakage of K^+ in the resting state, and relates the steady decrease of membrane resistance in time with potassium leakage. Other data obtained concern the value of the resting potential, the spike height and the associated ion changes. The membrane resistance of cardiac Purkinje fibers falls^{278, 279} to about 1/50–1/100 of the resting value during the early (spike) part of the complex potential changes, recovers and becomes larger than normal during the plateau and falls in the rapid termination of the plateau. There is rectification at the membrane, and block of activity by anodal pulses. The impedance measurements indicate rapid but incomplete "inactivation" of the sodium permeability change (cf. Hodgkin¹³⁰ and later discussion in this review) and perhaps a slow rise of potassium permeability.

Preliminary experiments by Grundfest et al.¹¹⁶ show that the impedance change of activity is always associated with nearly the same point on the rising phase of the spike, even though the latter is slowed in low external sodium solution. The effect of changing the ionic milieu is rapid for cleaned giant axons. The impedance change is smaller the lower the concentration of sodium in the external fluid. With time, the impedance change in normal sea water also diminishes, but the experiments have not progressed far enough for correlation of this phenomenon with the resting membrane resistance or with the slow ionic changes in the nerve fiber. Membrane resistance changes in nerve fibers as a result of cathodal and anodal polarization are described by Strohl,²⁴⁶ and Albe-Fessard⁵ has studied the impedance changes as well as the electric circuit properties of the electric organ. Discussion of the important data of Fatt and Katz⁸⁴ will be reserved for a subsequent section.

It would appear to the reviewer that in the very near future there should come a reevaluation of the equivalent circuit components of nerve in terms of their physical reality. The equivalent circuit is a convenient instrument for analyzing the behavior of nerve, just as it is often convenient for analyzing the behavior of mechanical systems and others. Even the most sophisticated users of the equivalent circuit in neurophysiology must,

however, be constantly on guard not to overstep the boundaries where the "equivalence" of the electrical and physiologic systems is valid.

Membrane resistance is perhaps the easiest "electrical" property to analyze in terms of its physiologic meaning. The experiments described above¹¹⁶ demonstrate that the membrane resistance changes at a relatively fixed time in reference to the onset of the spike. It is also a function of the concentration of the external sodium. Its meaning as the measure for transport of ions across the surface barrier of the cell—membrane in our parlance—is generally recognized. The "membrane capacity" is a somewhat more abstruse element. It might represent the ability of the membrane to absorb ions.

If the above is correct, the concept of the decay of the spike, or of the end plate potential, cannot be viewed as merely a passive event depending upon the time constant, CR, of the equivalent circuit, although it can be usefully described as such for working purposes.⁸⁴ Rectification and inductance are other equivalent electrical descriptions of phenomena which have their specific physiologic bases in the bioelectric generator.⁵⁶⁻⁵⁸ What seems to the reviewer an oversimplified use of the inductance term will be discussed in connection with the section on transmission and junctional properties.

One of the many merits of Hodgkin's review¹³⁰ is its treatment of the equivalent circuit elements in term of their meaning for the dominant events of the ion movements during the early phase of the electrical activity. The work of Shanes²³³⁻²³⁶ and others indicates that the later electrical events are also associated with ion movements, particularly the movement of potassium. The physiologic changes which cause or permit these various movements are not yet clear, however.

The Role of Ions in the Resting Potentials

That the resting potential of the cell is determined primarily by these, as yet unknown, mechanisms which maintain in the interior ionic distribution different from the external medium, seems to be well established. The earlier success of Hodgkin and Katz^{131e} in giving mathematical expression for the relation between external potassium concentration and the resting potential has been followed by Huxley and Stämpfli's¹³⁹ very ingenious measurements on frog single nerve fibers. The precision of measurements and their fit to a theoretically derived expression are very good. In the single myelinated fibers the effects of the change in external potassium concentration is evidenced as a change in the resting potential in about 1 sec. Similarly, the effect of changing the sodium concentration is as rapidly visible in a modification of the spike height, but changes in that ion have little effect on the resting potential. Lithium to a considerable degree can

substitute for sodium. Schriever²³⁰ discusses the bioelectric potentials as a Donnan effect.

Role of the Sheaths

The hindrance to ion movements by the sheaths of myelinated nerve trunks has been more decisively reaffirmed.^{65, 87} This work countered Lorente de Nó's¹⁷⁵ criticism of earlier experiments⁸⁶ that removing the sheath altered the physiologic properties of the underlying nerve fibers. In the new work, the sheaths were removed in such a fashion that they could be again slipped over the "desheathed" nerve trunk. The "resheathed" nerves regained, or very nearly so, the sluggish behavior of the resting potential of the intact nerve towards ionic change in the external fluid. The sheath is also a barrier to the entry of antihistamines and related compounds⁶⁶ which are able to block conduction of nerve without changing the resting potential.

Lundberg¹⁸¹⁻¹⁸⁵ presents data on the effects of various ions or their lack, anoxia and temperature on the electrotonic potentials and excitability of frog nerve fibers and spinal roots. While the figures indicate a methodology remarkably similar to that of Lorente de Nó, some of the data and conclusions are quite divergent. Roots and "desheathed" nerves behave differently, or have properties different from those of "sheathed" nerves, both as regards the electrotonic potentials and the effects of ions. Lundberg thus agrees with Feng and Liu, as well as with Rashbass and Rushton,²¹² who it will be recalled asserted that the polarizability of the sheaths caused serious distortions in Lorente de Nó's recorded electrotonic potentials, falsifying his theory. The reader is referred to Hodgkin¹³⁰ for additional discussion on this and the following topic.

Substitution for Sodium by Organic Ions

Lundberg's data¹⁸² also show that spinal root C fibers are even less resistant than are the A fibers to deprivation of Na^+ .¹⁷⁴ In discussion of Hodgkin's paper at the International Physiological Congress,^{131a} the reviewer mentioned that autonomic C fibers become either inexcitable or are capable of giving only very rare, slow, small responses to electrical stimulation. This poor ability to respond may be due to a substitution of Na^+ in the nerve sheaths by the ethyl-ammonium compounds; a low concentration of Na^+ thus being made available would make possible occasional, but very weak responses by the fibers of smallest diameter, which might, because of their size, obtain sufficient sodium for occasional activity. Lundberg's data and our own are thus in accord. On the other hand, Lorente de Nó¹⁷⁷ believes that there is a gradation in properties of axons; that roots behave differently from their peripheral extensions. Such differences on a subtle

scale may and perhaps do exist. Whether the reactivity of the bioelectric mechanism to stimuli might partake of such differences is another matter. That bioelectric tissues can apparently survive, and as Lorente de N6 claims, even improve the size of their response when Na^+ is substituted by the ammonium salts has received support, however, from observations of Fatt and Katz⁸⁵ in crustacean muscle fibers. Choline chloride, however, acts here in the same way as do the ethyl ammonium compounds, to prolong and increase the response, and this is not compatible with Lorente de N6's findings.

Dynamics of Ion Distribution

The mechanism for the large difference in ionic composition between the interior of the cell and its exterior, while as yet unknown, has been the subject of much speculation. These are summarized well in the references given at the beginning of this chapter. Steinbach²⁴² believes that there may be a sodium binding system in muscle. An interesting new possibility is suggested by the work of Shedlovsky²³⁷ on protochemical cells (as differentiated from electrochemical cells). On the basis of his analysis, Shedlovsky has made useful "protode" cells. This analysis, in its present state, would not serve to construct a model of the cell membrane, since the protode cell is dependent upon a restraining membrane (in Shedlovsky's case, the glass electrode wall) which permits transfer only of protons. In the nerve cell, however, ion passage across the membrane is relatively unselective, the resting conditions being determined by another mechanism, probably "sodium pumping," as well as by the Donnan effect. The remarkable specificity of the membrane change during activity is a further stumbling block, but it need not be fatal. Shedlovsky's proton transfer system apparently has much in common with the mode of action of various types of ion exchangers (as pointed out by him at a colloquium at Woods Hole in the summer of 1951). Several hypotheses which regard the nerve membrane essentially as an ion exchange system are now in development (independently, by F. Bergmann and by G. Ling). Hodgkin and his colleagues^{130, 131c} stress the possible importance of calcium ions, as does the mathematical paper of Karreman¹⁴¹ and the earlier paper by Monnier.¹⁹⁰

Whatever the result of these theories may be, we are in debt to Keynes and his colleague Lewis for valuable quantitative information on the movement of ions across the axonal membrane.¹⁴⁶⁻¹⁴⁷ The kinetics of the resting exchange of radioactive potassium have been worked out for *carcinus* axons, as has the leakage of K^+ on stimulation. The problem was further attacked for *sepia* axons in which inward and outward flux of both Na^+ and K^+ during rest and activity have been determined. The data are too numerous to be detailed here, and for the many implications of this work,

readers should consult the original papers and Hodgkin's review. In summary, this work is entirely consistent with other data accumulated in the past few years, which show that both Na^+ and K^+ exchange through the resting axonal membrane; that during activity of the nerve fiber, K^+ is lost and Na^+ is gained. The absolute amounts of ion exchange associated with electrical activity are remarkably consistent for a number of methods used by different investigators. For giant axons, Na^+ gain per impulse, per cm^2 of membrane varies from 3.5–4.5 $\mu\mu\text{mol}$, and the K^+ loss from 3.0 to 4.3 $\mu\mu\text{mol}$ under the same conditions. Keynes^{146b} also presents reasons for supporting the view that a sodium pump mechanism does exist. (See also Ussing and Zerahn.²⁶⁹) Other new evidence for a sodium pump is derived from experiments with frog skin.²⁶⁸⁻²⁶⁹ Keynes and Lewis¹⁴⁸ have additionally employed the very ingenious method of "activation analysis"^{240, 264} for determining the ionic content of *sepia* axons and their changes with time and with activity. The method is based upon exposure of the tissues to intense neutron bombardment and measurement with appropriate filters of the radiation from the activated samples. From the immediate Beta and Gamma counts so obtained and from a comparison of the radiation from simultaneously activated samples of Na^+ and K^+ salts, the concentrations of the ions in the nerve are derived directly. P, S, and Cl determinations are further possible by differential measurements taking account of the decay curves of the various ions. The technic enables measurements of as little as 0.3 μg Na and 3 μg K, with an error of ± 2 per cent.

- The data obtained by this method show that with time there is a gain of Na and a loss of K. But after an initial change, following removal of the nerve from the animal, the ion movement is relatively small (if any) for the first 4 hours (see their figs. 7 and 8), particularly if the data on short stretches of nerve (those of 21 mm length and less; the filled circles of their figures) are eliminated, as one might justifiably do, to minimize killed end effects. The actual data accordingly show much more stability of the internal ionic milieu than might have been supposed. Rather similar results have been obtained in our own laboratory (unpublished), by flame photometer analyses of squid axons. Van Harreveld²⁷² finds that in rabbit nerve there is a loss of potassium during the first two hours but little thereafter. Hodgkin¹³⁰ has tabulated available data for distribution of K, Na and Cl in excitable tissues.

Overshoot of the Spike and Its Relation to Sodium Permeability

The dependence of the manifestation of the spike upon a change in the permeability of the membrane to Na^+ has been still further established in the past year. In vertebrate single nerve fibers,¹³⁷⁻¹³⁹ in the Purkinje fibers

of the mammalian heart,^{73*} in the frog ventricle,²⁸⁵ and in mammalian motoneurons,³⁶ the spike has been observed to overshoot the value of the resting potential. The extant list of data (with the exception of Eccles') has been collected by Huxley and Stämpfli¹³⁸ and by Hodgkin¹³⁰ and is impressive. Weidman²⁷⁷ has confirmed the existence of the overshoot in squid giant axons and Fatt and Katz⁸⁴ its presence in frog muscle fibers. These authors, as well as Nastuk,¹⁹⁸ have found an interesting effect of the end plate on the muscle fiber spike. At the end plate, the muscle fiber spike is smaller than when it is recorded with the microelectrode elsewhere in the active fiber. Fatt and Katz⁸⁴ explain the effect as due to "short circuiting" of the muscle fiber potential by the low resistance of the active end plate membrane. Both groups of workers find a "step" in the spike recorded at the end plate. This represents the e.p.p. preceding the activation of the propagation activity. A "hump" on the falling phase is considered by Nastuk to be the sign of a remnant e.p.p., but Fatt and Katz explain it as a consequence of the short circuiting effect.

That the overshoot is dependent upon the external $[Na^+]$ as earlier demonstrated by Hodgkin and Katz^{131c} and by Nastuk and Hodgkin²⁰⁰ has now been confirmed for myelinated frog nerve fibers by Huxley and Stämpfli.¹³⁹ The reviewer cannot refrain from expressing his admiration for the ingenious circuit analysis which permitted these workers to develop this new method for measuring resting and action potentials of nerve fibers thus far unmanageably small for attack by the microelectrode technic. Their data demonstrate very good proportionality between the active membrane potential and external $[Na^+]$ with a theoretically expected slope of 58 mv.

Additional data for the Na^+ hypothesis is provided by the measurements of ion transfer during activity^{131b} which were mentioned earlier. We have recently added further to the evidence, by demonstrating that the membrane resistance change during activity becomes smaller when giant axons are bathed in solutions of low Na^+ .¹¹⁶

The Spike and the Sequence of Ion Movements

The method of "zero membrane voltage difference" has yielded Hodgkin, Huxley and Katz^{130, 131c} some important information on the temporal course of the movement of ions during activity. The papers referred to, however, are only preliminary. Hodgkin¹³⁰ states that some difficulties have turned

* A similar overshoot and response form has been observed in spontaneously active tissue culture of chick embryo heart muscle in our laboratory (F. A. Mettler, H. Grundfest, S. M. Crain and M. R. Murray, Amer. Neurol. A., 77th meeting, 1952). We have also obtained an overshoot in the unit response in electroplax of the eel (unpublished), as have Keynes and Martins-Ferreira.

up in following through the implications of the data. In outline, the results indicate a rapid transient increase in sodium permeability when the membrane is critically depolarized. This phase is succeeded by a later but longer lasting increase of the potassium permeability. In the figures of Hodgkin, Huxley and Katz the first phase is a period of current flowing inward transported by the entering Na^+ . This is followed by a K^+ current flowing outward. By decreasing the concentration of the external sodium, the first inward phase of current flow could be first decreased in magnitude. When the $[\text{Na}^+_{\text{o}}]$ fell to the level of the $[\text{Na}^+_{\text{i}}]$ the first phase of current flow was absent. On lowering the concentration of external sodium below that of the interior, the first phase of current reversed, becoming, as the later phase, an outward flow.

Hodgkin states: "The assumption that the increase in sodium permeability is transient implies that the nerve must contain a mechanism which gradually reduces sodium permeability to a low level. This process will be described by the 'inactivator.' " As will be seen, this is also the conclusion of Nachmansohn and his colleagues, who additionally postulate a specific mechanism for the "inactivation" process. While the "zero membrane voltage difference" method does not give an exact picture of the processes involved in the spike in the sense that a spike is prevented from appearing, it suggests that "sodium entry predominates during the rising phase while potassium exit predominates during the falling phase." Hodgkin also says: "This suggests that the membrane must undergo a remarkable series of permeability changes." This conservatively worded statement of the complexity of the underlying phenomena must suffice for the present.

THE ROLE OF NEUROCHEMICAL INTERMEDIATES IN NERVE ACTIVITY

Acetylcholine as the Neurochemical Intermediate

The mechanism postulated for the role of acetylcholine in electrical activity has recently undergone considerable evolution. At the First Macy Foundation Conference, the writer suggested direct participation of the esterase in the structure of the membrane.^{112, 113} Nachmansohn, however, proposed as an alternative the existence of a "receptor protein" located in the membrane.¹⁹⁵ According to the most recent formulation of his theory, therefore, acetylcholine is released from its normal bound form by current flow, either from an external stimulating source or from the local circuit. The energy requirement for this process is quite small. Grundfest¹¹² has calculated from Marmont's¹⁸⁹ data that the electrical quantity involved is 10^{-9} coulombs. The same value has been recently obtained by Fatt and Katz⁸⁴ for the muscle end plate. Hodgkin,¹⁹⁰ on the other hand, calculates that the spike represents at least 150×10^{-9} coulombs. Yet, the "safety

factor" of nerve is less than 10, as can be deduced from the measurements of Marmont¹⁸⁹ and Hodgkin et al.^{131c} that the critical level of the local response is about 15 mv. The discrepancy, therefore, requires that a local rapid expenditure of energy be involved. This could be derived, as Nachmansohn has stressed,¹⁹⁵ from the chemical reactions of the energy transforming cycle. The reviewer had emphasized earlier the need for "amplifier" action at the synapse.¹¹¹

The acetylcholine freed by the local circuit energy combines reversibly with the receptor protein to initiate the increased sodium permeability of the membrane. However, the presence of the powerful esterase quickly destroys the acetylcholine, restoring the original state. Formally, at least, the concept outlined here is that of a mechanism which is suitable to the theory proposed by Hodgkin and his colleagues.

Evidence that Nachmansohn's receptor protein concept is to be preferred to that which I had proposed has recently come from joint work which we have carried out in collaboration with C. Y. Kao and Robert Chambers.¹¹⁸ The purpose of this work was to see whether, as we suspected should be the case, curare and prostigmine, which are ineffective on nerve when applied externally, cause block of activity when injected into the axon. This proved to be the case. The experiments, of course, support Nachmansohn's view that the nerve membrane is a selective barrier for certain substances of particular structural form (the quaternary ammonium salts) and helps to explain differences of pharmacologic action at different loci of the nervous and effector systems.

However, the quantitative aspects of these results gave new data. Curare³ blocks conduction when injected into the axon in the surprisingly small quantity of 10^{-5} μ g. Stilbamidine, a substance which interferes with the neurochemical mechanism (because of powerful, paired cationic charges spaced approximately $14 \text{ \AA}$ apart), apparently in the same mode as does curare, is also effective in approximately the same quantity (10^{-4} μ g). Prostigmine and eserine, both very effective inhibitors of acetylcholinesterase, on the other hand, act only in much higher concentrations (0.1 to 1 μ g). The site and, perhaps, mode of action of the different blocking agents, therefore, appears different.

These experiments show that if a neurochemical mechanism exists, as seems very likely, it is more complicated than had been earlier supposed, and is consistent with Nachmansohn's suggestion of a receptor protein, structurally and functionally part of the excitable membrane. This is not, however, the only possible formulation. Data on the processes of enzymatic activity and its inhibition are largely derived from *in vitro* experiments. It is also possible, for example, that in the cell the acetylcholine esterase

is part of a more complex membrane component, and that the binding forces of curare and similarly acting compounds exert their effects on this complex.

This problem is of considerable immediate interest because it is also concerned with the resting potential and because through this aspect it is susceptible to experimental attack. It has been shown²⁶⁶ and confirmed in our own experiments on giant axons and crab nerve (Grundfest, Hendley and Guttman, unpublished), that DFP and eserine produce little or no change in the resting potential in the course of blocking nerve activity. It is clear now that the resting potential is probably determined by a process different from that which produces the action potential.^{130, 131c} Nevertheless, if intracellular release of acetylcholine is the neurochemical trigger for the momentary change of membrane sodium permeability, its accumulation in the presence of esterase inactivators should, on the basis of the earlier simple theory, cause a change in the resting potential. This follows from the demonstration^{117a, 220} that the esterase inhibitors cause changes in the ion permeability of the membrane, and from the fact¹¹⁸ that acetylcholine itself is a strong inactivator of nerve. Unfortunately, in our preliminary experiments with microinjection, it was not possible to measure the resting potentials also. Experiments are under way now which it is hoped will be able to explain this situation.

At the end plate, externally applied acetylcholine does change the resting potential^{83, 199} and it appears likely that the effect is by means of a change of the sodium permeability of the membrane. This effect may be due to the permeability of the junctional membrane to the quaternary salts, as Nachmansohn believes. On the other hand, it is perhaps possible that the junctional membrane is characterized by the existence both at its interior and on its external aspect of a "receptor" complex of the type mentioned above. Further experiments of the type reported by Burns and Paton⁴⁷ studying the effect of various blocking agents which act with and without depolarization—in combination with our increasing knowledge of the intricate structural chemical mechanisms of these compounds—will be of value.

The reader's attention is called to the more recent data which have come from Nachmansohn's laboratory, particularly through the work of Wilson¹⁹⁷ regarding the analysis of the structure and bonding charges of the neurochemical system. On the basis of these physico-chemical deductions, a number of predictions have been made and verified. Since they as yet are largely in the field of *in vitro* enzyme studies, the reader will have to seek their details in the review cited.¹⁹⁷

One prediction, however, is of immediate neurophysiologic interest. Stil-

bamidine which is used therapeutically in trypanosomiasis, has as mentioned above, a charge distribution like that of curare. Stilbamidine, however, is less completely dissociated at neutral pH than is curare. The free base, present at pH 7 in less than 1 per cent, should be able to penetrate the nerve membrane and the drug should, therefore, accumulate in the interior, eventually to cause block. This was found to be the case.²⁶ More recent joint studies (unpublished from Nachmansohn's and my own laboratories in collaboration with Professor Snapper) have compared the blocking effectiveness of stilbamidine and of 2-hydroxy stilbamidine at different pH. The results are in agreement with expectations from the dissociation curves of these substances.

The Role of Oxidation Reduction Systems

Arvanitaki and Chalazonitis have persevered at an ambitious and painstaking program of relating the metabolic events and systems of cells and axons to the mechanism of their electrical activity. Their theory was presented at the Paris colloquium of 1949,¹⁸ and suggests that bioelectric phenomena arise from the chain of redox levels of the respiratory catalysts. The more recent papers of this series^{20, 52} are concerned with the identification and localization of various respiratory redox systems. The reviewer believes that this ingenious theory has a serious flaw; redox systems involving electron transfer are not capable of producing current flow and electrical work in the absence of a metallic conductor as an electron acceptor-donor.*

Thus, if the redox systems were the generators of some type of bioelectric potential, propagation of activity and transmission across junction (phenomena to which Mme. Arvanitaki-Chalazonitis has herself so importantly contributed) would have to get along without intervention of the local circuit mechanism. If redox potentials cannot of themselves yield electrical work in the absence of a metallic conductor, the theory of Arvanitaki and Chalazonitis must include a transfer mechanism which energizes another system or set of systems acting via an ionic transfer mechanism to yield the resting potential and the propagated action potential. These intermediaries would then be equivalent to the sodium pump mechanism for the resting cell and to the series of transient changes in sodium and potassium permeability which are initiated during the action potential.†

* I wish to thank Dr. Theodore Shedlovsky for confirming the correctness of this statement. Dr. I. B. Wilson also points out that not all redox systems are capable of transferring electrons to metallic conductors.

† Insofar as Lorente de N6's hypothesis^{172, 173} also involves a metabolic reaction chain, it partakes of the same criticism.

Chemical Correlates with Bioelectric Potentials at Rest and in Activity

Acetylcholine is released²⁴ from the perfused salivary glands of *octopus* when the nerves are stimulated. The number of reacting cold spots is increased²⁵ by acetylcholine-like substances and prostigmine, decreased by adrenaline and atropine, while ergotamine, dibenamine, and hydergine have no effect. Cholinergic substances also lower the thresholds to thermally induced pain.²⁴⁰ A histamine like substance is said to be released on autonomic stimulation of skin nerves, which sensitizes the sensory receptors and causes an increase of spontaneous discharges from the skin.¹¹⁹

Shanes²³³⁻²³⁶ has carried on further studies on the changes in the delayed potentials of nerve activity (positive and negative after-potentials) and of the resting potentials, combining a variety of tools (anoxia, "stabilizers" like cocaine, the veratrine alkaloids which behave as "unstabilizers," calcium excess or deficiency), with determinations of K^+ movement, in a number of technically very skillful procedures. He concludes²³⁵ that the measured "potassium shifts are in the proper direction and of the correct order of magnitude to account for the negative and positive after-potentials in terms of potassium accumulation or depletion in the extracellular space." These are valuable results and make a strong case for Shanes' views which are summarized with economy in the review previously mentioned.²³⁴ The present writer must, however, take issue with his good friend regarding a conclusion in the opening statement of that review which is neither necessary nor sufficient. Referring to the data of Hodgkin and his associates on the relation of spike production to sodium entry Shanes says: "As recognized by those investigators, the data are either highly indirect and dependent on a number of assumptions or seriously dissociated in time from the bioelectrical events assumed to be involved." The data at hand when Shanes presented his paper were on the contrary characterized by a high degree of directness, when one considers correlations between rapid, indirect electrical and slow, direct chemical measurements of events as Hodgkin¹³⁰ has pointed out (cf. p. 339). The approach used by the Cambridge group and others is similar to that of Shanes but deals primarily with the early events of bioelectric activity, while Shanes thus far deals only with later phases of nerve activity. The studies of Shanes, therefore, need not, and in comprehensive theory should not, be in contradiction to the sodium theory of Hodgkin and his colleagues. Feng et al.⁸⁹ have provided additional evidence that resting potential changes are correlated with potassium gain and loss. Potassium loss occurs in asphyxia of mammalian nerves.²⁷²

Feng et al.⁸⁸ and Shanes²³⁵ have also made the important observation that failure of nerve activity in nitrogen can be repeatedly and quickly removed by washing the nerve with oxygen free fluid. Shanes finds that

recovery is considerably slower when oxygen gas is introduced without at the same time washing the nerve. Our experience has been in agreement with this that mammalian nerves stimulated frequently in a warm, moist gas atmosphere also often fail, but are restored to full activity by momentary immersion in the Ringer's solution. The explanation of the phenomena offered by these workers appears reasonable. The potassium, leaking out of the nerve fibers during anoxia, accumulates in the extracellular fluid and leads to inexcitability. Washing with oxygen free solution dilutes the accumulated potassium and removes the inexcitability. Shanes' observation that recovery takes place slowly if oxygen gas alone is introduced would then mean that under this condition the excess external potassium only slowly reenters the cells.

Other aspects can only be mentioned very briefly. Gallego and Lorente de N^o⁹⁸ agree that lithium can restore conduction in nerve, thus substituting for sodium to this extent, but that it cannot replace the role of sodium in the L fraction^{172, 173} or in the "nerve reaction." Lorente de N^o believes that in other respects the role of sodium is not specific.¹⁷⁶ This would appear likely if one only considers the long term changes of the "nerve reaction." Cocaine¹⁷⁸ has a two-fold action.

The effects of potassium and rubidium on depolarization of muscle has been studied by Sandow and Mandel,²²³ who find that both ions act in a manner consistent with classical membrane theory. The authors disagree with Lorente de N^o^{172, 173} as to the need for a new theory and with Feng and Liu⁸⁶ as to the mode of action of rubidium. Lundberg,¹⁸⁴ on the other hand, finds some differences between potassium and rubidium as regard electrotonic potentials. Heavy metal ions block nerve conduction reversibly.⁴⁹ This effect was also observed in earlier work (unpublished) in the reviewer's laboratory, uranium nitrate being used as the blocking agent on giant axons of squid. The importance of these results lies in the findings of others (e.g. Rothstein and Meier²²¹) that the effect of uranium ion is on the surface of the cell membrane.

Another dispute seems to be brewing; this time on the effects of certain metabolic inhibitors on the resting potential. Lorente de N^o^{172, 173} claimed that iodoacetamide delayed the anoxic depolarization of nerve. Liu¹⁶⁹ denies this and believes that Lorente de N^o's results which were also contrary to those of earlier observers were due to experimental errors.

A series of preliminary notes on metabolic requirement of nerves and cells will only be referred to here^{28, 48, 59, 164} as well as a preliminary report on enzymatic and metabolic properties of cells and components.¹ Nerves of birds are particularly sensitive to anoxia.²⁰³ After ischemia, nerves become hyperexcitable and respond repetitively.¹⁵⁷ Oxygen lack and CO₂ excess affect monosynaptic and polysynaptic spinal reflexes differently.¹⁵⁰

Photochemical and Related Effects

Photochemical effects have been employed to seek insight into the chemical mechanisms of nerve activity. Booth et al.³² find that irradiation of a node of a single frog fiber with ultraviolet of wavelengths below 320 m μ raises the threshold and then blocks conduction. On irradiating the internodes, the effect on the neighboring node is opposite, the threshold falling. An action spectrum of the nodal effect has been obtained and the authors believe that thiamin might be one of the substances involved in the photochemically affected process, which they suggest is linked with the sodium permeability mechanism. Arvanitaki and Chalazonitis in neurons of adult *Aplysia*^{16b} find a heme-protein and a carotene-protein which are photo-dynamically activated. The effect is a change in the frequency of cellular activity. It is oxygen dependent. In neurons of young *Aplysia*, on the other hand, they find¹⁷ a carotenoid and a "chlorophyll" pigment. Irradiation of the former leads to cessation of rhythmic activity or its slowing. The opposite effect is obtained when the "chlorophyll" pigment is selectively irradiated.

BIOELECTRIC FUNCTION AND STRUCTURAL CORRELATES

The Process of Excitation

This review will not examine critically various theories of the excitation process, although a considerable number of publications have recently appeared on the subject. The reader is referred to the work of Tasaki and his colleagues²⁵⁶⁻²⁶² which is the most extensive and where frequently a number of excitation parameters have been determined on the same single fiber. Other work is by LeFevre,¹⁶⁵ Lussier and Rushton,¹⁸⁶ Sato^{224, 225} and Schoepfle.²²³ Yamagiwa²⁹⁰⁻²⁹⁴ has published studies of Lillie's iron wire model which treat with many aspects of nerve function (temperature effects, saltatory conduction, facilitation and inhibition and junctional excitability). An interesting paper by Karreman¹⁴¹ combines a mathematical discussion with some specific postulates regarding the kinetics of membrane permeability to a hypothetical system of ionic changes in which are invoked Ca, P and K.

The very interesting phenomenon termed "amortissement" (damping)^{191, 192} and the effects of CO₂ on threshold, and on subthreshold events in nerve^{62, 158-160, 166-168} are under study in Monnier's laboratory. The implications of these phenomena for the basic processes of nerve activity would seem to be connected with the metabolic events which are interrelated with nerve function as studied by Shanes, Lorente de Nó and others.

Conduction

Since my last review, there has been some controversy regarding the reality of saltatory conduction. Autrum and Schneider^{22, 23, 227} have denied its validity because they found that: (a) the impulse could jump a gap in contradiction to earlier evidence which the reviewer had considered as most conclusive for saltatory conduction, and (b) manipulation of the internode stretch, by cutting, pressure or cold produced a block. A re-examination of the first line of evidence by Frankenhauser and Schneider²⁴ has shown that the earlier contradictory results were due to an experimental fault. The amplifiers used to record the earlier data had a low grid leak resistor which of itself acted as a shunt to carry the local circuit current for the active regions to the region beyond the air gap. This is a confirmation, in other words, of many earlier "bridge" experiments. The new work also shows that the second type of contradictory evidence was not conclusive. The authors, therefore, believe that the present evidence is consistent with the possibility of saltatory conduction. The contrary evidence resulting from the experiment of cooling the internode has also been refuted.¹³³

Laporte¹⁶² working on intact preparations of frog spinal nerves and particularly on intact lateral line nerves of carp, chosen because of long internodes,²⁶³ claims that saltatory conduction is disproved by his experiments. The conduction velocity is uniform along the nerve, and the spike displays no discontinuities in magnitude or shape. Laporte also presents the argument common to Lorente de N6's laboratory that study of single nerve fibers dissected from the whole nerve is responsible for erroneous results. This may be true in specific cases, but is not a tenable generality, despite the finality of Laporte's statement that "the results presented . . . do not justify a discussion of the evidence obtained by previous investigators who have worked with dissected out single fibers. All that can be said is that dissected out single fibers and undissected nerve fibers seem to have different properties. . . ." The reviewer believes this is a reversion to a philosophic discussion on artefacts in biology which has now become antiquated by virtue of many kinds of factual evidence.

Hodgkin¹³⁰ believes the criticism of Laporte (like the earlier criticism of Rosenblueth et al.²¹⁹), "appears to rest on a misunderstanding," of deductions from the theory of saltatory conduction. Conduction time plotted against conduction distance should not show significant deviation from linearity, while the amplitude of the spike "should not decrease by more than 10 per cent as the recording electrode is moved from a node to the middle of an internode," (Huxley, unpublished). On the other hand, Stämpfli and Zotterman²⁴¹ conclude that Laporte's failure to find a periodicity in spike form

was due to technical errors, and they were able to demonstrate periodicity of spike form in the intact dorsocutaneous frog nerve.

Tasaki²⁵⁵ has further demonstrated that the local circuit current of one nerve fiber can excite another, properly positioned for effective entry of the current at its nodes. Lussier and Rushton¹⁸⁷ find that in the frog nerve trunk the current enters and leaves entirely through the nodes. Field⁹¹ reports that prussian blue diffuses slowly along nerve fibers, but is taken up much more rapidly at the nodes.

Bodian³¹ has added to the earlier evidence that nodes exist in the central nervous system, and finds in several species that the nodal spacing is proportional to fiber diameter. In summary, this reviewer believes that all present evidence is strongly in favor of saltatory conduction.

The Local Response and Mechanisms of Junctional Transmission

A graded local response has been clearly demonstrated in many kinds of nerve fibers and in junctional tissues. Hodgkin¹³⁰ discusses the evidence and its implications. Recent evidence for its presence in vertebrate nerve fibers is given.^{137, 217, 218, 229} Eccles and his colleagues, in a preliminary publication,³⁶ and in the 1951 Adam Miller Lecture by Eccles, have reported on their results with an intracellular microelectrode inside the cat motoneuron. According to Eccles (Adam Miller Lecture) excitatory presynaptic impulses set up the classical local response type of synaptic potential, while the direct inhibitory action by other presynaptic afferents causes a symmetrical but oppositely directed electrical change of the synaptic membrane. He therefore concludes, in line with his most recent trend of thought,⁷⁷ that synaptic excitation is achieved through a neurohumoral mechanism. The "excitatory" afferent fibers on this view release an "excitatory" substance while the "inhibitory" action of other afferents is caused by an "inhibitory" substance. To the argument of this reviewer that Arvanitaki's^{16a} positive anodal local response (apparently also observed by Rosenblueth and Garcia-Ramos²¹⁷ in mammalian nerves) may be related to the "inhibition" membrane response of the motoneuron, Eccles (personal communication) has responded with his interpretation of the anodal response as given in his review of 1948.⁷⁶ There, Eccles explains the anodal local response as a result of the inductive properties of nerve⁵⁶⁻⁵⁸ apparently making the analogy with the "ringing circuit" of electrical engineering. If this reviewer understands the case to be so, Eccles' argument would appear to be incorrect. The "inductive" properties of nerve fibers are so only from formal analogy but are produced by a mechanism entirely different from that of electrical circuits.^{111, 112} Hodgkin¹³⁰ puts the facts very well in saying: "It is not difficult to see that changes in permeability to potassium should lead to behaviour similar to that of an inductance."

Accordingly, the oscillatory responses of nerve fibers or cells *must* be associated with permeability changes in the membrane, and not with the behavior of electrical analogies. If this is true, Arvanitaki's anodal local response is indicative of permeability changes associated with hyperpolarization of the membrane. It would then follow that Eccles' finding of an hyperpolarizing effect on the motoneuron is evidence of the same type of phenomenon—a response to a local anodal presynaptic focus. Postulating a neurohumoral "inhibitory" substance would then be unnecessary. With the elimination of the need for an "inhibitory" neurohumoral would also go the need for an "excitatory" one. As was pointed out in my earlier review of this series,¹¹² the evidence of Eccles for an excitatory neurohumor is not inconsistent with the interpretation of local circuit synaptic excitation and intracellular neurochemical activity.

The reviewer believes, therefore, that following through the consequences of the assumption¹¹¹ that the synaptic response acts in the nature of an amplifier,* and consideration of Arvanitaki's local anodal response as a manifestation of an active process at the membrane, make unnecessary the successive surrenders by Eccles of an electrical transmitter mechanism at the myoneural junctions and at the central nervous synapses. The operation of these two factors may also be used to explain the puzzling electrical changes in, and inhibition of motor activity by the inhibitory fibers of invertebrates.^{145, 155}

Eccles' own demonstration³⁶ that the motoneuron soma responds with a spike which has an overshoot, would imply, if his view on the transmitter system be accepted, that the membrane of the soma has similar properties on both its sides. The overshoot of the spike in antidromic activation must be explained on the generally accepted mechanism discussed earlier, as affecting the membrane permeability to sodium by the cathodal foci at the soma membrane. The inhibitory and excitatory neurohumors must also affect the membrane in the same way from the outside, as Fatt and Katz⁸⁴ have also postulated, which would call for a similar permeability changing mechanism accessible from the outside of the cell.

Kuffler has also marshalled his arguments against electrical transmission at the myoneural junction.^{153, 154} His primary evidence comes from ingenious experiments on stimulation of nerve fibers very close to the end plate. Since the nerve impulse then travels in both directions (towards the end plate and away from it), Kuffler believes (and Eccles,⁷⁷ agrees) that the conditions do not provide a "source" for current flow and therefore neuro-

* In their very interesting paper on the bioelectric mechanism of synaptic transmission, Arvanitaki and Chalazonitis¹⁹ suggest that the specific response of the cell, which I called "amplification," may be related to the high concentration of mitochondria and other cellular structures which are associated with enzyme activity.

muscular transmission should not occur. Since the end plate potential and transmission nevertheless are manifested, Kuffler believes this is strong evidence for release of a neurohumoral transmitter substance in association with the nerve impulse.

To the reviewer this conclusion does not necessarily follow. Within the last millimeter or so of its course the nerve fiber divides very profusely to innervate the motor end plates. The dromic conduction velocity will therefore tend to become exceedingly slow as compared with the antidromic. The spike at the terminals may last somewhat longer than does the receding antidromic spike. If the terminal arborizations behave as do the arborizations which the dendrites of neurons represent, some of this extensive branching system will not be thrown into activity because of the presence of local blocks. These three conditions would thus cause establishment of a terminal sink and a resultant cathodal focus in the subjacent junctional tissue. Arguments against electrical transmission derived from presumed inadequacy of the current flow seems to me less relevant because the synaptic response acts as an amplifier. These experiments, therefore, do not disprove electrical transmission. The brief note by Dun⁷⁵ is to the point here, since it stresses the possible importance of the factor of terminal arborization at a junction. He suggests that blocked pre-fibers may be the direct inhibitory fibers. Various interaction effects of the arborizations may be expected. A number of other possible effects are also suggested.

Less potent arguments in favor of a chemical transmitter Kuffler deduces from a number of other experiments.¹⁵⁴ Some of them (e.g., action of ChE inhibitors and the inhibitory nerve action of invertebrate nerves) have been mentioned and evaluated earlier in the present review. The absence of electrical changes in the end plate by electrotonus caused by subthreshold stimulation of the nerve and alteration in the after potentials of the nerve can be explained in part by assuming an insufficient sensitivity of the recording mechanism; either by reason of the geometry of the recording system in relation to the site of the generator or by reason of the relation of the recording electrode to the volume conductor. These objections (presented earlier by the reviewer to Kuffler in discussions) have also been raised by Lorente de Nó.¹⁵³ Another type of evidence, derived from the change in the form of the end plate potential, during and after the passage of an intercurrent spike produced by stimulating the muscle fiber directly, is explicable on the basis of the data of Fatt and Katz⁸⁴ which demonstrate the "short circuiting" properties of the end plate on the response of the muscle fiber and imply a reciprocal effect from the fiber to the end plate.

Fatt and Katz⁸⁴ have published a very extensive analysis of the frog end plate potential carried out with the aid of glass microelectrode recording. Here the reviewer will confine his attention to that aspect of the work

which deals with the transmitter mechanism. To some extent, this work supercedes conclusions reached by Fatt⁸³ in another important paper. The end plate is found not to be directly excitable and this region also differs from the surrounding muscle fiber surface in being highly sensitive to chemical stimulants.

The latter finding is consonant with the physico-chemical interpretations of the pharmacologic data by Nachmansohn.¹⁹⁵ The reviewer, however, tends to be conservative in his opinions on the first point. Electrical excitability seems (he takes refuge in the qualifying phase) to be a general property of all excitable tissues which have been adequately studied. Thus, smooth muscle fibers were at one time considered inexcitable, and yet are now known to respond to electrical stimuli.

Primarily, it would appear, because of the supposed electrical inexcitability of the end plate, Fatt and Katz postulate that the end plate is activated not by the local circuit of the motor nerve impulse but by release of acetylcholine from the nerve terminations. The acetylcholine is then supposed to alter the permeability of the junctional membrane to sodium. Except for the assumption that the acetylcholine acts from the exterior, the theory of Fatt and Katz is similar to Nachmansohn's suggestion on the mode of action of acetylcholine, though these authors do not mention the similarity. The views of Fatt and Katz would not explain the identical permeability events within the nerve fiber, and, therefore, the reviewer, who on the question of nervous and synaptic activity is (he hopes) an enlightened unitarian, prefers the unifying hypothesis of Nachmansohn.

Bullock⁴⁴ has pointed out that the synaptic responses of invertebrate nerves are comparable in duration with the duration of the propagated spikes and shorter than the synaptic responses of the vertebrate junctions. Fatt and Katz believe that the rising phase of the vertebrate e.p.p. is determined by the "transmitter" neurohumor, while the decay is determined by the RC product of the membrane, essentially as a passive phenomenon. In keeping with this view, are the physical constants they observe for the membrane. The capacity is high (approx. $8 \mu\text{f}/\text{cm}^2$).

We have recently begun an intensive study of the phenomena in the electroplax of the electric eel. Germane to the discussion here, is the demonstration that in perfused surviving slices,¹¹ and in the single unit, nerve stimulation produces a prolonged excitatory effect, which may last over 300 msec when the single arriving nerve impulse does not fire the electroplax. This is manifested by the full response of the units to a second subsequent stimulus. Slight traces of the effect may be observed in slow repetitive stimulation (1 or 2 stimuli/sec.) and appear to be responsible for the "iterative" character of the response of electroplax to nerve stimu-

lation. The curve of excitability rises to a maximum fairly slowly (about 10 msec) and falls even more slowly (half time about 50 msec.).

It appears from our available data that this effect is indicative of an end plate potential. Eserine, prostigmine and other esterase inhibitors change the facilitative curve, before producing block.

Acetylcholine has an electromotor effect on the end plate, but not on the muscle fibers.^{83, 199} Decamethonium has a similar action.⁴⁷ (For further pharmacologic studies, see Chapter IV.)

Properties of Electric Organs

Problems in the theory of the mode of action of the electric organ were summarized by the Fessards and Chagas.⁹ A recent paper by Mme. Albe-Fessard and her colleagues¹⁰ give a very useful, rapid summary of much of the current physiologic information as well as new data. The unit responds to direct stimulation and to stimuli applied to nerves with spikes of about 1 msec duration. Thresholds of excitation are high. Although neural activation is the normally necessary pathway, accelerated recruitment of active units by combined action of the nerve impulses and of electrotonic effect on the inactive units from those already active is proposed. This would account for the high velocity of the progression of the activity along the animal (250 msec; much slower than earlier figures, but still higher than the velocities in the nerves). Albe-Fessard has further studied the physical properties of the organ;⁶ the nature of the response;⁴ its modification by applied currents;⁶ and the central control of the activity.^{7*}

Properties of Nerve Fibers

Gasser⁹⁹ has brought forward an authoritative demonstration that the unmyelinated afferent fibers of the cat have a different type of action potential from that of the autonomic C fibers. After the spike, there follows a positive potential—which Gasser terms “post spike positivity”—of long duration. This may be converted into “post spike negativity,” but neither form is said to be the classical after potential. The mammalian nerve fibers thus are composed of four types. The larger myelinated A fiber and the

* Reference has already been made to some of our own recent results with the electric tissue. R. D. Keynes has recently published a preliminary account of his independent and somewhat earlier studies (R. D. Keynes and H. Martins-Ferreira, to be published in *J. Physiol.* 116, 1952). These are entirely concerned with the unit plaque as a bioelectric generator. The data of Keynes and Martins-Ferreira and our own are in basic agreement that the unit is specialized insofar as only part of the cell boundary (the innervated caudal surface) acts as a reversibly highly sodium permeable system. It is this adaptation which permits the addition of the voltages from each unit generator to form the high potentials observed from many units in series.

autonomic unmyelinated fibers (designated by Gasser as sC) show a sequence of negative and positive potentials after the spike. The small thinly myelinated, autonomic B fibers and the unmyelinated afferent fibers (now designated as d.r. C) lack the negative component after the spike, though in both types of fibers a negativity (after potential or "post spike") may be elicited. Earlier indications that dorsal root C fibers might be in a separate category were obtained on the basis of a "positive after effect" associated with the spike by Bishop;²⁹ on the basis of the curve of recovery of excitability by Grundfest and Gasser;¹¹⁵ and on the basis of repetitive responsiveness to long electrical and thermal stimuli by v. Euler.⁸²

Gasser's distinction between after-potentials and post-spike potentials, while no doubt valid by the criteria he employs, raises a very important question regarding the processes which underlie these potentials. Lorente de Nó's interpretations^{172, 173} are well known and have been discussed in my earlier review.¹¹² As indicated there, and also earlier in this review, some of his experimental evidence must be rejected. His concepts of the electrochemical mechanism, insofar as they partake of the redox concept of Arvanitaki and Chalazonites, are also subject to the criticism I have made of the latter. Nevertheless, there remains a considerable body of experimental data regarding the subtle metabolic processes of nerve which must be taken into account in a complete description of nerve function. The data of Shanes and of Feng and their colleagues need also to be considered in this relation. Only a preliminary attempt can be indicated here.

The sodium hypothesis as the explanation of the spike carries with it associated postulates on the movement of potassium. Unless other ions also become implicated late negativity at the exterior of the nerve fiber probably always means movement of potassium outward. The reverse ion movement would then be associated with external positivity. This is consistent with the data of Shanes for the late components of the action potential. Gasser's distinction between after potentials and post-spike potentials would then indicate that there must be additional factors which affect excitability and other properties of nerve during the manifestation of ionic movements. Bullock⁴⁴ has stressed that responsiveness and propagation may in fact be to some extent dissociated.

Gasser has also surmounted the exceedingly difficult task of measuring the diameter of the afferent unmyelinated fibers. From the fiber counts he has reconstructed, with satisfactory results, the recorded spikes under different experimental conditions by assuming that the velocity of conduction and the size of the potential contributed by each fiber vary directly as the diameter of the fiber.

Ambache¹² has reported remarkable differences of sensitivity to Botulinus toxin in different nerves. The autonomic blocking action of the toxin is

said to be through an effect on cholinergic preganglionic nerve fibers, whether they be in the sympathetic or parasympathetic divisions. The adrenergic fibers are said to be two or three hundred times more resistant to the toxin. Differences in histamine and noradrenalin content of myelinated and unmyelinated nerve fibers are also reported.²¹³ Gasteiger¹⁰¹ reports that susceptibility to Beta radiation of mammalian nerve fibers discloses differences in fibers of the A groups, which seem to be correlated with the sizes of the fibers and may perhaps reflect their relative size as targets. Heat (and ultrasound which appears to affect nerve through the heat energy) has been used to indicate differential properties of bullfrog nerve fibers.¹⁶¹ With slow application of heat there is at first a block of conduction (beginning at 40° C) which is completed at 43–44° C, but in the range of 44–45° C a large proportion of the fibers regain ability to conduct, which is lost again between 45–46° C. In the first stage of blocking the smaller fibers of the A group go out first (the order being γ , β , α). In the second stage, block develops in the reverse order. These stages are missed in rapid heating. B fibers are blocked at about 44° C and C fibers at 45° C. But susceptibility to irreversible block is in the order A, C, B, and the authors suggest that pure B fiber preparation could be thus obtained. Lundberg¹⁸⁵ finds that the after potentials are larger in sensory A fibers as compared with those of motor A fibers in nerve frog.

In connection with the claims that peripheral and central portions of peripheral nerves have different properties,¹⁷⁷ other workers⁵⁰ find that fatigued rabbit nerve fibers with intact blood supply have the same recovery time for conduction velocities and spike height at the periphery and centrally. Nerves with intact blood supply recover after one or two hours of stimulation at very high rates (300–1000/sec). From the records for the highest rate of stimulation it is apparent that alternation is taking place and that the individual fibers are responding at rates below 1000/sec.

Malcolm¹⁸⁸ has studied the conduction velocity in human nerves *in situ*. It is considerably lower (50–80 m/sec) than might be expected from experiments with animals,³⁷ even if account is taken of the possible effects of the lower skin temperature. Low values are similarly observed in measurements for the knee and ankle jerk.

Phenomena in Degenerating and Regenerating Nerves

Young,²⁹⁵ in a very useful summary, discusses the question of what determines the specific properties of cells and fibers. Young stresses that "factors acting down from the cell body and up from the periphery" influence fiber size. Possibly, physiologists are too prone to neglect the influences of interrelations of structures and functions of the organism. An interesting example of such an influence is the report of Koshtoyantz¹⁵²

that the chromatographic patterns of the glycogen of muscle change during denervation and back again on reinnervation. In the innervated muscle there appear to be several varieties of glycogens.* In the denervated muscle only a single type occurs. Sunderland²⁵⁰ has summarized the regeneration phenomena in human peripheral nerves.

Gallego⁹⁷ compares the effects of sodium deprivation on normal and degenerating nerve fibers. In degenerating nerve fibers, loss of excitability is faster than in normal nerve fibers. Van Harreveld's²⁷¹ finding that destruction of myelin leads to greater potassium leakage appears to be related to this effect. Bouman et al.³³ have proposed a new electrodiagnostic test of denervation, which depends on measuring the relation between frequency of stimulation and the intensity of the stimulus. De Smedt^{68, 69} has studied changes of electrical excitability in degenerating and regenerating nerves and correlates the effects of these changes with the fibrillations of denervated muscles.⁷⁰ Bowden and Sholl³⁴ describe the rate of functional recovery following radial nerve lesions and Rexed and Rexed²¹⁴ of corneal nerves. Lubinska¹⁸⁰ from studies of the effects of temperature (frog and toad) concludes that the "latent period" of regeneration and the growth of the nerve fibers are due to different processes.

The effects of ischemic lesions on nerve have been reviewed by Richards,²¹⁵ who believes that tourniquet paralysis is also a result of the additional pressure. Attention of neurophysiologists should be called to an interesting clinical finding in tourniquet and pressure paralyses. It has been long known to clinicians that this paralysis is associated with local block of the nerve fibers, but that below the block (which may last three months¹¹ or more, according to my colleague Dr. J. Moldaver) the nerve remains electrically excitable. This has been recently confirmed by Moldaver, who has also studied the loss and return of sensory modalities (unpublished). The continued functional survival of a nerve below a region of prolonged block is an interesting matter for the relation between nerve structure and function. Its clinical implications stress the need for caution by neurosurgeons (pointed out by wartime experiments) in treating nerve injuries in continuity.²¹⁰ Sunderland²⁵¹ reports some remarkable histologic changes produced in nerve by implanting foreign materials. These changes, confined to short segments, do not adversely affect function.

This review cannot encompass a survey of the extensive work on muscle action potentials. In relation to the topic here under discussion, however, should be mentioned the paper of Pinnelli and Buchthal,²⁰⁵ which de-

* Another demonstration of such interaction is the requirement that a certain amount of nervous tissue be present in the amputation surface in order to permit regeneration of an amputated limb in the newt. A recent paper giving earlier references is that of R. L. Sidman and M. Singer (*Am. J. Physiol.* 165:257, 1951).

scribes changes in the muscle action potential in poliomyelitis. Notable is the increase in the amplitude of the motor unit spike. A still more remarkable change has been observed²⁸⁹ in muscles reinnervated after peripheral nerve lesions. The amplitudes of some of the motor unit spikes increase as much as twenty-fold, in comparison with the homologous unaffected muscles. The possibility that this increase in amplitude was a result of reinnervation of many more muscle fibers by an excessively branching regenerating nerve fiber was considered. This must be the case for initially totally denervated muscles. In the light of similar observations in poliomyelitis and other diseases affecting motoneurons, however, it was concluded that enlargement of the motor unit by new branches from intact motor nerve fibers²⁷⁰ was the probable explanation for the general case of motoneuron diseases.

NEUROPHYSIOLOGY OF SENSE ORGANS

Study of sensory reception by electrophysiologic methods seems to be on the increase. Hensel and Zotterman, in a series of papers,¹²¹⁻¹²⁶ have shown that the cold receptors of the tongue in the cat and dog respond to an absolute temperature change, and not, as classical theory would have it, to a gradient of temperatures. Menthol¹²⁴ is a specific stimulant for cold receptors, but its effect can be compensated for by warming the animal. Not too surprisingly, they find¹²⁵ that some types of mechanoreceptors of the tongue are also responsive to cold, but the temperatures required are more extreme than those needed to stimulate the cold receptors. This finding is in line with current ideas that most of the cutaneous sensations represent a mixture of activity of different kinds of sensory receptors. Sweet taste fibers in the dog¹⁴ and a receptor responding to water¹³ for the frog's tongue are reported. Itch sensation¹⁰² seem to have two neural components. A prickling sensation is carried in large fibers, and can be differentially eliminated by ischemic anesthesia. A burning sensation which remains is carried in small fibers (probably unmyelinated). This is differentially blocked by cocaine anesthesia, when the prickling sensation alone remains. The authors suggest a spinal mechanism for involvement of a considerable hyperesthetic zone around the directly affected skin. This would invoke excitation of intraspinal pools of neurons by the afferent bombardment which would make the impulses arriving from the hyperesthetic zone more easily perceived. The explanation has been indicated as a possibility by Grundfest and Magnes.¹¹⁷ Sinclair and Hinshaw^{238, 239} have restudied the sensory dissociation produced by procaine, compression and cold blocks of nerve.

Gray and his colleagues¹⁰⁴⁻¹⁰⁸ have devised a useful technic for the study of Pacinian corpuscles and of frog skin touch receptors. A piezoelectric

mechanical stimulator enables them to apply graded stimuli of varied form. Mesenteric corpuscles are activated by a mechanical movement of only 0.5μ and $100 \mu\text{sec}$ duration. Repetitive discharges are rare and adaptation is rapid. Linearly rising stimuli show considerable difference between the excitable properties of touch receptors and of Pacinian corpuscles. Scott²³¹ finds that oscillating mechanical stimuli yield distinctions between different Pacinian corpuscles. Hardy et al.¹²⁰ find a difference between the number of just noticeable steps for the pain of deep pressure on the forehead and the cutaneous pain evoked by their radiant thermal stimulator. A preliminary note by Adrian³ reports that different kinds of olfactory receptors (as judged by differences in spike height of their nerves) have characteristic thresholds for different kinds of olfactory stimulants. He also finds some by no means complete localization in the olfactory pathway.

Only some of the "vagal stretch receptors" function in this capacity.²⁷⁶ An analysis of the afferent vagal fibers in relation to their role in respiratory reflexes can only be mentioned here.^{286, 288} Large, slowly adapting sensory fibers of the larynx seem to be also associated with the control of respiratory activity.¹⁵ Two papers^{72, 284} analyze respiratory afferent activity in terms of measurements of unit electrical activity. Cooper et al.⁶¹ report the characteristics of oculomotor nerve discharges from activity of the external eye muscles. There is a rapid discharge (as high as 300/sec), little adaptation and prompt cessation as befits the extremely important eye muscles. The elasmobranch labyrinth is being studied intensively with electrophysiological methods.¹⁷⁹ In *Limulus*,²⁷⁴ the photoreceptor elements exhibit a slowly rising excitation to a subliminal stimulus. This is followed by refractoriness and slow recovery therefrom when the subliminal stimulus is turned off.

The lateral line organs of the fish have been studied by two groups. *Fundulus* reacts to sound stimuli up to 200–300 cps.²⁴⁸ Strong spontaneous activity is present. An extensive study of the Japanese eel¹⁴²⁻¹⁴⁴ brings additional data. The authors point out that histologically the lateral line organ bears a marked similarity to Corti's organ of the mammal. The reader will find much more information in these papers than can be presented here.

POTENTIALS OF CELLS IN THE SPINAL CORD AND GANGLIA

The preliminary note by Eccles³⁶ on motoneuron potentials has already been discussed. Svaetichin, using his low resistance microelectrodes,^{252, 253} has studied cells of the frog and cat spinal ganglia.²⁵⁴ A resting potential of 50–90 mv is reported, but the spike response of the cell is of about the same height. The absence of an overshoot, if confirmed by subsequent work, is the only exception known thus far. Nor do the records show after potentials, or a local response like that found by Eccles in motoneurons. Svaetichin has analyzed the response which is obtained by recording from

the surface of the dorsal root ganglion in the cells, as the afferent impulse arrives first in the myelinated portion of the fiber in the vicinity of the cells (the M response), then in its unmyelinated initial segment (the I response), and finally in the cell (the P response). The last two components can be blocked by repetitive activity. Dun⁷⁴ reports a related blocking phenomenon, also in the dorsal root ganglia of frog.

Lloyd^{170, 171} has again demonstrated his mastery of the volume conductor conditions of the spinal cord by an analysis of the motoneuron response to antidromic stimuli, as recorded from various aspects of the surface of the spinal cord, within it and from the roots. As in Svaetichin's data, there are responses referable to the myelinated fiber within the spinal cord (M response), of its unmyelinated segment (I response) and the soma response (Lloyd calls this the b deflection). Added to these, however, is a d deflection which is referred to activity of the dendrites, is slowly conducted, variable in its development and lasts a long time. The M response is resistant to asphyxia and has a short refractory period as is to be expected of the myelinated fiber. Blocks may occur anywhere along the remaining pathway, and particularly in the dendritic arborizations which extend high into the dorsum of the cord. The sequence of late potentials is analyzed, in terms of the current flows in the volume conductor, into an early state of soma positivity (lasting about 40 msec) and soma negativity (lasting for about 120 msec). Correlations are made between the flow of these currents and excitability. Some discrepancies which remain between these results and those of Eccles and his group,^{80, 81} and particularly in the light of Eccles' new data on cell potentials, will have to be adjusted by further experiments. Another study of potentials of the spinal cord, that of Fuortes,⁹⁶ emphasizes the relation of the potentials to the morphologic organization.

The results of Chang⁵⁴ which indicate slow conduction in the dendritic ramifications of the cerebral cortex will only be mentioned here for their relations with Lloyd's findings. The same observer⁵⁵ reports that strychnine has no effect on the dendrite spikes. Strychnine also has no synchronizing effect²⁷⁵ in dorsal root and stellate ganglia, in the oculomotor and Edinger-Westphal nuclei and on cells of the lateral horn. Repetitive firing was observed from the lateral horn cells. Frankenhauser,⁹³ on the basis of experimental work, warns of the limitations of "strychnine neuronography." Scherer,²²⁶ on the other hand, finds it useful in study of spinal reflexes. Kirstein's¹⁵⁰ use of asphyxia and CO₂ for differential study of spinal reflex activity should be mentioned also in this connection.

ELECTROPHYSIOLOGY OF PERIPHERAL INTEGRATING MECHANISMS

Through the work of Bullock, Turner and Wiersma, the invertebrate peripheral nervous system is providing new information on the anatomic and functional adaptations which the organism may develop for the pur-

pose of integrative mechanisms. The hermit crab, *Eupagurus bernhardus* L, has opener muscles,²⁸¹ the fibers of which are innervated only by a single nerve fiber. Yet the response of the muscle can be either fast or slow, as with doubly-innervated muscles. The difference is considered in relation to the reported absence of propagation in crustacean muscles and to different types of nerve endings from the same nerve fiber.

In the crayfish, *Cambarus*, certain motor fibers make synaptic connection in sequence at four different loci.²⁸³ When block occurred at one of the synapses, transmission was usually also prevented at any of the more central synapses. The interpretation and physiologic significance of this phenomenon are discussed by the authors. Wiersma²⁸² has also published a useful study of the innervation of the leg muscles of the lobster. Prosser et al.²⁰⁹ have described the action potentials associated with slow and fast responses of invertebrate non-striated muscles. While the situation is still not entirely clear, the authors believe that the responses are mediated by two kinds of muscle fibers and two kinds of nerve fibers.

The existence of "unpolarized synapses" (i.e., capable of transmission in either direction) has been demonstrated again in various invertebrates by a number of workers,^{42-45, 267, 283} and the presence or absence of synaptic responses should be an interesting subject for study. Bullock⁴⁴ has called attention to the polychaete giant fibers and provides detailed studies of their "natural and quasi-artificial synapses." Nicol²⁰¹ is also studying the physiology of the sabellid worms. (See also Bullock's recent papers.)

Kuffler and his colleagues^{134, 135, 156} have published the detailed analysis of the function of the small ventral root motor fibers of mammals. These fibers innervate the muscle spindles and, perhaps by altering tension of the intrafusal fibers, change the sensitivity of the spindles to stretch. This mechanism serves as an aid to control the precision of the mechanical response. The additional control mechanism provided by the presence of two kinds of stretch receptors is studied in another of their papers. The spindle receptors have a low threshold and cease to discharge on contraction of the muscle. The tendon receptors have a high threshold, and their rate of discharge increase during contraction. Both types are innervated by large afferent fibers conducting at velocities of 90-100 msec (range 60-125 msec).

Variations of the level of excitability of the motoneurons by means of the afferent reports of the degree of stretch of the muscles is shown and studied by Granit and Ström.¹⁰³ A preliminary report¹⁶³ shows another important local integrative mechanism. Arrival of group I impulses facilitates monosynaptic reflexes of the synergic and inhibits those of the antagonist muscles. The reverse effect is to be seen in the disynaptic reflexes. The authors suggest that this may be the neurophysiologic mechanism of

the lengthening reaction. Post-tetanic potentiation is evaluated for its physiologic importance.²⁴⁷ It is concluded that it cannot be of great quantitative significance because it is a phenomenon observed after firing the afferents at very high frequencies and is difficult to produce by physiologic ranges of stimuli.

REFERENCES

- ¹ Abood, L., Cavanaugh, M., Tschirgi, R. D., and Gerard, R. W.: Metabolic and pharmacologic studies in glia and nerve cells and components. *Federation Proc.* 10:3, 1951.
- ² Adey, W. R.: The nervous system of the earthworm *Megascolex*. *J. Comp. Neurol.* 94:57, 1951.
- ³ Adrian, E. D.: Differential sensitivity of olfactory receptors. *J. Physiol.* 115:42P, 1951.
- ⁴ Albe-Fessard, D.: Les caractères de la décharge des poissons électriques. *Arch. Sc. Physiol.* 4:299, 1950.
- ⁵ —: Propriétés électriques passive du tissu, électrogène des poissons électriques. *Arch. Sc. Physiol.* 4:413, 1950.
- ⁶ —: Modification de l'activité des organes électriques par des courants d'origine extérieure. *Arch. Sc. Physiol.* 5:45, 1951.
- ⁷ —: Données sur les caractères de la commande centrale de la décharge chez la torpille et chez la raie. *Arch. Sc. Physiol.* 5:197, 1951.
- ⁸ —, and Chagas, C.: Action d'une substance curarisante sur la décharge électrique de l'*Electrophorus electricus*. *Compt. rend. Soc. de biol.* 145:248, 1951.
- ⁹ —, Chagas C. and Fessard, A.: Premières données sur les potentiels de membrane des électroplaxes et leurs modifications électrotoniques. *Arch. Sc. Physiol.* 3:643, 1949.
- ¹⁰ —, Chagas, C., Couceiro, A., and Fessard, A.: Characteristics of responses from electrogenic tissue in *electrophorus electricus*. *J. Neurophysiol.* 14:243, 1951.
- ¹¹ Altamirano-Orrego, M., Coates, C. W., Grundfest, H., Nachmansohn, D., and Wilson, I. B.: Activity of electroplax of electric eel. *Federation Proc.* 11:4, 1952.
- ¹² Ambache, N.: A further study of the action of *Clostridium botulinum* toxin upon different types of autonomic nerve fibers. *J. Physiol.* 113:1, 1951.
- ¹³ Andersson, B. and Zotterman, Y.: Nerve endings in the frog's tongue responding to pure water. 18th Internat. Physiol. Congress, 75, 1950.
- ¹⁴ —, Landgren, S., Olson, L., and Zotterman, Y.: The sweet taste fibers of the dog. *Acta physiol Scandinav.* 21:105, 1950.
- ¹⁵ Andrew, B. L.: The sensory innervation of the larynx. 18th Internat. Physiol. Congress, 75, 1950.
- ¹⁶ a. Arvanitaki, A.: Réactions au stimulus anodique. Étude de la réponse électrique locale de signe positif. Observations sur l'axone isolé de sepie. *J. de physiol. et de path. gén.* 38:146, 1941-1943.
b. Arvanitaki, A. and Chalazonitis, N.: Reactions bioélectriques neuroniques à la photoactivation spécifique d'une hème protéine et d'une carotène-protéine. *Arch. Sc. Physiol.* 3:27, 1949.
- ¹⁷ —: Inhibition ou excitation des potentiels neuroniques à la photoactivation distincte de deux chromoprotéides (caroténöide et chlorophyllien). *Arch. Sc. Physiol.* 3:45, 1949.

- ¹⁸ —: Catalyse respiratoire et potentiels bioélectriques. Arch. Sc. Physiol. 3:303, 1949.
- ¹⁹ —: Prototypes d'interactions neuroniques et transmissions synaptiques. Données bioélectriques de préparations cellulaires. Arch. Sc. Physiol. 3:547, 1949.
- ²⁰ —: Recherches sur la répartition de quelques catalyseurs respiratoires dans l'espace cellulaire (axone géant et soma neuronique de *Sepia*). Arch. Sc. Physiol. 5:207, 1951.
- ²¹ —: Effets narcotiques sur les biopotentiels neuroniques et sur la catalyse respiratoire. Mécanisme de la Narcose, Centre National de la Recherche Scientifique (CNRS) Paris. 195-216, 1951.
- ²² Antrum, H. and Schneider, D.: Der kälteblock der einzelnen markhaltigen nervenfaser. Naturwiss. 1:21, 1950.
- ²³ —: Die blockierung der erregungsleitung in einzelnen markhaltigen nervenfaseren durch lokalen druck. Naturwiss. 2:46, 1950.
- ²⁴ Bacq, Z. M. and Ghiretti, F.: Acetylcholine release during nerve stimulation of the perfused posterior salivary glands of *octopus vulgaris* and *o. macropus*. J. Physiol. 114:51P, 1951.
- ²⁵ Barron, E. S. G. (ed.): Modern Trends in Physiology and Biochemistry. New York, Academic Press, 1952.
- ²⁶ Bergmann, F., Wilson, I. B., and Nachmansohn, D.: The inhibitory effect of stilbamidine, curare and related compounds and its relationship to the active groups of acetylcholine esterase. Action of stilbamidine upon nerve impulse conduction. Biochem. et biophys. acta. 6:217, 1950.
- ²⁷ Berry, W. K. and Lovatt, E. C.: Cholinesterase and neuromuscular block. J. Physiol. 115:46, 1951.
- ²⁸ Bing, H. I. and Skouby, A. P.: Sensitization of cold receptors by substances with acetylcholine effect. Acta physiol. Scandinav. 21:286, 1950.
- ²⁹ Bishop, G. H.: The action potentials at normal and depressed regions of non-myelinated fibers, with special reference to the 'monophasic' lead. J. Cell & Comp. Physiol. 5:151, 1934.
- ³⁰ —: Excitability. Trans. 2nd Conf. on Nerve Impulse. New York, Josiah Macy, Jr., Foundation, 1951.
- ³¹ Bodian, D.: A note on nodes of Ranvier in the central nervous system. J. Comp. Neurol. 94:475, 1951.
- ³² Booth, F., von Muralt, A. and Stämpfli, R.: The photochemical action of ultra-violet light on isolated single nerve fibres. Helvet physiol. acta. 8:110, 1950.
- ³³ Bouman, H. D., Baumgarten, B. S., and Shaffer, K. J.: Frequency intensity curves of human muscle: a new method for quantitative electrodiagnosis. Federation Proc. 10:18, 1951.
- ³⁴ Bowden, R. E. M. and Sholl, D. A.: The advance of functional recovery after radial nerve lesions in man. Brain. 73:251, 1950.
- ³⁵ Brazier, M. A. B.: The Electrical Activity of the Nervous System. New York, Macmillan Co., 1951.
- ³⁶ Brink, F., Jr.: Anesthetizing action. Trans. 2nd. Conf. on Nerve Impulse. New York, Josiah Macy, Jr., Foundation, 1951.
- ³⁷ Brock, L. G., Coombs, J. S., and Eccles, J. C.: Action potentials of motoneurons with intracellular electrode. Proc. Univ. Otago Med. School. 29:14, 1951.
- ³⁷ Brock, L. G., Eccles, J. C., and Rall, W.: Experimental investigations on the afferent fibers in muscle nerves. Proc. Roy. Soc. Med. 138:453, 1951.

- ³⁸ Bronk, D. W. and Brink, F.: On the mechanism connecting impulse conduction and oxygen metabolism in peripheral nerve. *Federation Proc.* 10:19, 1951.
- ³⁹ Brooks, C. McC. and Fuortes, M. G. F.: Central excitation and inhibition. *Trans. 2nd Conf. on Nerve Impulse*. New York, Josiah Macy, Jr., Foundation, 1951.
- ⁴⁰ Brown, H. and Goldberg, E.: The neutron pile as a tool in quantitative analysis; the gallium and palladium content of iron meteorites. *Science*. 109:347, 1949.
- ⁴¹ Bullock, T. H.: Conduction and transmission of nerve impulses. *Ann. Rev. Physiol.* 13:261, 1951.
- ⁴² —: The course of fatigue in single nerve fibers and junction. 18th Internat. Physiol. Congress, 134, 1950.
- ⁴³ —: Facilitation of conduction rate in nerve fibers. *J. Physiol.* 114:89, 1951.
- ⁴⁴ —: Properties of some natural and quasi-artificial synapses in polychaetes. *J. Comp. Neurol.* (In press).
- ⁴⁵ —, and Turner, R. S.: Events associated with conduction failure in nerve fibers. *J. Cell. & Comp. Physiol.* 36:59, 1950.
- ⁴⁶ Burgen, A. S. V. and Terroux, K. G.: Membrane potentials of cat auricle and their response to pain sympathomimetic drugs. *Federation Proc.* 10:21, 1951.
- ⁴⁷ Burns, B. D. and Paton, W. D. M.: Depolarization of the motor end-plate by decamethonium and acetylcholine. *J. Physiol.* 115:41, 1951.
- ⁴⁸ Carlson, F. D. and Brink, F., Jr.: Dependence of steady-state rate of oxygen metabolism as frequency of conducted impulses in peripheral nerve. *Federation Proc.* 10:24, 1951.
- ⁴⁹ del Castillo-Nicolau, J. and Hufschmidt, H. J.: Reversible poisoning of nerve fibres by heavy metal ions. *Nature*. 167:146, 1951.
- ⁵⁰ Causey, G. and Schoepfle, G. M.: Fatigue of mammalian nerve in relation to the cell body and vascular supply. *J. Physiol.* 115:143, 1951.
- ⁵¹ Chagas, C., Couceiro, A., and Martin-Ferreira, H., Resultats de quelques expériences de perfusion de l'organe électrique d'*Electrophorous electricus* L. *Compt. rend. Soc. de biol.* 145:247, 1951.
- ⁵² Chalazonitis, N. and Arvanitaki, A.: Identification et localisation de quelques catalyseurs respiratoires dans le Neurone d'Aplysia. *Bull. Inst. Oceanograph.* 48:996, 1951.
- ⁵³ Chambers, R. and Kao, C. Y.: The physical state of the axoplasm in situ in the nerve of the squid mantle. *Biol. Bull.* 101:206, 1951.
- ⁵⁴ Chang, H. T.: Dendritic potentials of cortical neuron produced by direct electrical stimulation of the central cortex. *J. Neurophysiol.* 14:1, 1951.
- ⁵⁵ —: An observation on the effect of strychnine on the local cortical potentials. *J. Neurophysiol.* 14:23, 1951.
- ⁵⁶ Cole, K. S.: Some physical aspects of bioelectric phenomena. *Proc. Nat. Acad. sc.* 35:558, 1949.
- ⁵⁷ —: Dynamic electrical characteristics of the squid axon membrane. *Arch. Sc. Physiol.* 3:253, 1949.
- ⁵⁸ — and Baker, R. F.: Longitudinal impedance of the squid giant axon. *J. Gen. Physiol.* 24:171, 1941.
- ⁵⁹ Connelly, C. M.: Kinetics of increased oxygen consumption of activity in frog nerve. *Federation Proc.* 10:28, 1951.
- ⁶⁰ Conway, E. J.: Active transport of molecules and ions. 18th int. Physiol. Congress, 1950. Mimeographed unclassified technical report ONRL 101-50, American Embassy, London.

- ⁶¹ Cooper, S., Daniel, P. M., and Whitteridge, D.: Afferent impulses in the oculomotor nerve, from the extremities eye muscles. *J. Physiol.* 113:463, 1951.
- ⁶² a. Coraboeuf, E.: L'action particuliere du CO₂ sur le nerf myelinise et son independance a l'egard du pH. *Compt. rend. Soc. de biol.* 145:544, 1951.
b. —: Modification progressive des caracteristiques du nerf myelinise au cours du passage d'un courant continues sous-liminaire. *Compt. rend. Soc. de biol.* 145:927, 1951.
- ⁶³ Cragg, B. G.: The turgidity of giant axons. *J. Physiol.* 114:234, 1951.
- ⁶⁴ Crane, E. E.: Bioelectric potentials, their maintenance and function. *Progr. Biophys.* 1:85, 1950.
- ⁶⁵ Crescitelli, F.: Nerve sheaths as a barrier to the action of certain substances. *Am. J. Physiol.* 116:229, 1951.
- ⁶⁶ — and Geissman, J. A.: Certain effects of antihistamines and related compounds on frog nerve fibers. *Am. J. Physiol.* 164:509, 1951.
- ⁶⁷ Davson, H.: Textbook of General Physiology. Philadelphia, Blakiston, 1951.
- ⁶⁸ De Smedt, J. E.: Étude expérimentale de la dégénérescence wallérienne et de la réinnervation du muscle squelettique. I. Évolution de la constante de temps d'excitation. *Arch. internat. de physiol.* 58:23, 1950.
- ⁶⁹ —: Étude expérimentale de la dégénérescence wallérienne et de la réinnervation du muscle squelettique. II. Évolution de la constante de temps d'accommodation. *Arch. internat. de physiol.* 58:125, 1950.
- ⁷⁰ —: Pathogénie de la fibrillation du muscle squelettique dénervé. *Acta neurol. et psychiat. belg.* 4:179, 1950.
- ⁷¹ Dickinson, C. J.: Electrophysiological Technique. London, Electronic Engineering, 1950.
- ⁷² Dirken, M. N. J. and Woldring, S.: Unit activity in bulbar respiratory center. *J. Neurophysiol.* 14:211, 1951.
- ⁷³ Draper, M. H. and Weidmann, S.: Cardiac resting and action potentials recorded with an intracellular electrode. *J. Physiol.* 115:74, 1951.
- ⁷⁴ Dun, F. T.: Studies on the conduction of sensory impulses through the dorsal root ganglia in the frog. *J. Cell & Comp. Physiol.* 38:131, 1951.
- ⁷⁵ —: The terminal arborization of nerve fibers as an important factor in synaptic and neuromuscular transmission. *J. Cell & Comp. Physiol.* 38:133, 1951.
- ⁷⁶ Eccles, J. C.: Conduction and synaptic transmission in the nervous system. *Ann. Rev. Physiol.* 10:93, 1948.
- ⁷⁷ —: A review and restatement of the electrical hypotheses of synaptic excitatory and inhibitory action. *Arch. Sc. Physiol.* 3:567, 1949.
- ⁷⁸ —: Interpretation of action potentials evoked in the cerebral cortex. *EEG Clin. Neurophysiol.* 3:449, 1951.
- ⁷⁹ —: Adam Miller Lecture, New York 1951.
- ⁸⁰ — and Rall, W.: Effects induced in a monosynaptic reflex path by its activation. *J. Neurophysiol.* 14:353, 1951.
- ⁸¹ — and Rall, W.: Repetitive monosynaptic activation of motoneurons. *Proc. Roy. Soc.* 138:475, 1951.
- ⁸² v. Euler, C.: Differences between autonomic and somatic C fibers to stimulation with constant current. *Acta physiol. Scandinav.* 15:93, 1948.
- ⁸³ Fatt, P.: The electromotive action of acetylcholine at the motor end-plate. *J. Physiol.* 111:408, 1950.
- ⁸⁴ — and Katz, B.: An analysis of the end-plate potential recorded with intracellular electrode. *J. Physiol.* 115:320, 1951.

- ⁸⁵ — and Katz, B.: Conduction of impulses in crustacean muscle fibers. *J. Physiol.* 115:45P, 1951.
- ⁸⁶ Feng, T. P. and Liu, Y. M.: The connective tissue sheaths of nerve as effective diffusion barrier. *J. Cell. & Comp. Physiol.* 34:1, 1949.
- ⁸⁷ —: Further observations on the nerve sheath as a diffusion barrier. *Chinese J. Physiol.* 17:207, 1950.
- ⁸⁸ Feng, T. P., Hsu, C. H., and Liu, Y. M.: The mechanism of the recovery of nerve asphyxiated in nitrogen when washed with O₂-free Ringer. *Chinese J. Physiol.* 17:247, 1950.
- ⁸⁹ —: Correlation of potassium movement into and out of the nerve with its depolarization and repolarization. *Chinese J. Physiol.* 17:281, 1950.
- ⁹⁰ Fenn, W. O., Gerschmann, R., Fischer, G., Lacy, J., Bailly, M. D., and Wright, J. L.: Experiments on the role of K⁺ in the blocking of neuromuscular transmission by curare and other drugs. *J. Gen. Physiol.* 34:607, 1951.
- ⁹¹ Field, E. J.: Observations on the passage of Weed's prussian blue mixture along the axis cylinders and intra-fibre fluid of nerves. *J. Neurol., Neurosurg. & Psychiat.* 14:11, 1951.
- ⁹² Folch-Pi, J.: Metabolism. Trans. 2nd Conf. on Nerve Impulse. New York, Josiah Macy, Jr., Foundation, 1951.
- ⁹³ Frankenhaeuser, B.: Limitations of method of strychnine neuronography. *J. Neurophysiol.* 14:73, 1951.
- ⁹⁴ — and Schneider, B.: Some electrophysiological observations on isolated single myelinated nerve fibres (saltatory conduction). *J. Physiol.* 115:177, 1951.
- ⁹⁵ Fry, W. J. and Fry, R. B.: A possible mechanism involved in the conduction process of thin sheathed nerve fibers. *J. Cell & Comp. Physiol.* 36:229, 1950.
- ⁹⁶ Fuortes, M. G. F.: Potential changes of the spinal cord following different types of afferent excitation. *J. Physiol.* 113:372, 1951.
- ⁹⁷ Gallego, A.: Loss and recovery of excitability by normal and degenerating nerves deprived of sodium. *J. Gen. Physiol.* 35:129, 1951.
- ⁹⁸ — and Lorente de N6, R.: On the effect of ammonium and lithium ions upon frog nerve deprived of sodium. *J. Gen. Physiol.* 35:227, 1951.
- ⁹⁹ Gasser, H. S.: Unmyelinated fibers originating in dorsal root ganglia. *J. Gen. Physiol.* 33:651, 1950.
- ¹⁰⁰ — and Grundfest, H.: Axon diameters in relation to the spike dimensions and conduction velocity in mammalian A fibers. *Am. J. Physiol.* 127:393, 1939.
- ¹⁰¹ Gasteiger, E. L.: Effects of β rays on mammalian nerve action potentials. *Federation Proc.* 10:48, 1951.
- ¹⁰² Graham, D. T., Goodell, H., and Wolff, H. G.: Itch sensation in the skin: experimental observations on the neural mechanisms involved. 18th Internat. Physiol. Congress, 228, 1950.
- ¹⁰³ Granit, R. and Ström, G.: Autogenetic modulation of excitability of single ventral horn cells. *J. Neurophysiol.* 14:113, 1951.
- ¹⁰⁴ Gray, J. A. B., Malcolm, J. L., and Matthews, P. B. C.: Accommodation in certain sense endings and their nerves. 18th Internat. Physiol. Congress, 233, 1950.
- ¹⁰⁵ Gray, J. A. B. and Malcolm, J. L.: The initiation of nerve impulses by mesenteric Pacinian corpuscles. *Proc. Roy. Soc. London, s.B.* 137:96, 1950.
- ¹⁰⁶ —: The excitation of touch receptors in frog's skin. *J. Physiol.* 115:1, 1951.
- ¹⁰⁷ Gray, J. A. B. and Matthews, P. B. C.: Response of Pacinian corpuscles in the cat's toe. *J. Physiol.* 113:475, 1951:

- 108 —: A comparison of the adaptation of the Pacinian corpuscle with the accommodation of its own axon. *J. Physiol.* 114:454, 1951.
- 109 Gray, J. A. B. and Svaetichin, G.: Electrical properties of platinum tipped micro-electrodes in Ringer's solution. *Acta physiol. Scandinav.* 24:247, 1951.
- 110 Grenell, R. G. and Davies, P. W.: Effect of nembutal on the *in vivo* rate of oxygen consumption of the cerebral cortex. 18th Internat. Physiol. Congress, 239, 1950.
- 111 Grundfest, H.: Bioelectric potentials in the nervous system and in muscle. *Ann. Rev. Physiol.* 9:477, 1947.
- 112 —: General Neurophysiology. In Spiegel (ed.) *Progress in Neurology and Psychiatry*. Vol. V. New York, Grune & Stratton, 1950, p. 16.
- 113 —: Potentialities and limitations of electrophysiology. First Conf. on Nerve Impulse. New York, Josiah Macy, Jr. Foundation, 1950.
- 114 —: Mechanisms and properties in bioelectric potentials. In Barron (ed.) *Modern Trends in Physiology and Biochemistry*. New York, Academic Press, 1952.
- 115 — and Gasser, H. S.: Properties of C fibers in mammalian visceral nerves. *Am. J. Physiol.* 123:86, 1938.
- 116 — Guttman, R., Hendley, C. D., and Wilson, I. B.: Membrane resistance changes in the course of axonal spikes modified by low Na^+ concentration. *Science* (In press).
- 117 a. — and Magnes, J.: Excitability changes in dorsal roots produced by electrotonic effects from adjacent afferent activity. *Am. J. Physiol.* 164:502, 1951.
b. — and Nachmansohn, D.: Increased sodium entry into squid giant axons at high frequencies and during reversible inactivation of cholinesterase. *Federation Proc.* 9:53, 1950.
- 118 —, Nachmansohn, D., Kao, C. Y., and Chambers, R.: Mode of blocking axonal activity by curare and inhibitors of acetylcholinesterase. *Nature* 169:190, 1952.
- 119 Habgood, J. S.: Sensitization of sensory receptors in the frog's skin. *J. Physiol.* 111:195, 1950.
- 120 Hardy, J. D., Wolff, H. G., and Goodell, H.: Threshold and discrimination of differences in intensity of stimulus for deep pain. *Federation Proc.* 10:60, 1951.
- 121 Hensel, H. and Zotterman, Y.: The response of the cold receptors to constant cooling. *Acta physiol. Scandinav.* 22:96, 1951.
- 122 —: The persisting cold sensation. *Acta physiol. Scandinav.* 22:106, 1951.
- 123 —: Action potentials of cold fibers and intracutaneous gradient. *J. Neurophysiol.* 14:377, 1951.
- 124 —: The effect of menthol on the thermoreceptor. *Acta physiol. Scandinav.* 24:27, 1951.
- 125 —: The response of mechanoreceptors to thermal stimulation. *J. Physiol.* 115:16, 1951.
- 126 Hensel, H., Ström, L., and Zotterman, Y.: Electrophysiological measurements of depth of thermoreceptors. *J. Neurophysiol.* 14:423, 1951.
- 127 Hill, D. K.: The effect of stimulation on the opacity of a crustacean nerve trunk and its relation to fibre diameter. *J. Physiol.* 111:283, 1950.
- 128 —: The volume change resulting from stimulation of a giant nerve fibre. *J. Physiol.* 111:304, 1950.
- 129 Hodgkin, A. L.: Ionic exchange and electrical activity in nerve and muscle. 18th Internat. Physiol. Congress. Mimeographed unclassified Technical Report ONRL 101-50, p. 24, American Embassy, London.
- 130 —: The ionic basis of electrical activity in nerve and muscle. *Biol. Rev.* 26:339, 1951.

- ¹³¹ a — and Huxley, A. F.: Ionic exchange and electrical activity in nerve and muscle. 18th Internat. Physiol. Congress, p. 36, 1950.
- b —, Huxley, A. F., and Katz, B.: Ionic currents underlying activity in the giant axon of the squid. *Arch. Sc. Physiol.* 3:129, 1949.
- c — and Katz, B.: The effect of sodium ions on the electrical activity of the giant axon of the squid. *J. Physiol.* 108:37, 1949.
- ¹³² — and Keynes, R. D.: The mobility of potassium in the axis cylinder of a giant axon. 18th Internat. Physiol. Congress, p. 258, 1950.
- ¹³³ Hodler, J., Stämpfli, R., and Tasaki, I.: Über die wirkung internodaler abkühlung auf die erregungsleiteneig in der isolierten markhaltigen nervenfaser des frosches. *Arch. f. d. ges. Physiol.* 253:380, 1951.
- ¹³⁴ Hunt, C. C. and Kuffler, S. W.: Further study of efferent small-nerve fibres to mammalian muscle spindles. Multiple spindle innervation and activity during contraction. *J. Physiol.* 113:283, 1951.
- ¹³⁵ —: Stretch receptor discharges during muscle contraction. *J. Physiol.* 113:298, 1951.
- ¹³⁶ Hursh, J. B.: Conduction velocity and diameter of nerve fibers. *Am. J. Physiol.* 127:131, 1939.
- ¹³⁷ Huxley, A. F. and Stämpfli, R.: Direkte bestimmung des membranpotentials der markhaltigen nervenfaser in ruhe und erregung. *Helvet. physiol. acta.* 8:107, 1950.
- ¹³⁸ —: Direct determination of membrane resting potential and action potential in single myelinated nerve fibers. *J. Physiol.* 112:476, 1951.
- ¹³⁹ —: Effect of K^+ and Na^+ on resting and action potentials of single myelinated nerve fibers. *J. Physiol.* 112:496, 1951.
- ¹⁴⁰ Jacobs, M. H.: The measurement of cell permeability with particular reference to the erythrocyte. In Barron (ed.) *Modern Trends in Physiology and Biochemistry*. New York, Academic Press, 1952.
- ¹⁴¹ Karreman, G.: Contributions to the mathematical biology of excitation with particular emphasis on changes in membrane permeability and on threshold phenomena. *Bull. Math. & Biophys.* 13:189, 1951.
- ¹⁴² Katsuki, Y., Yoshino, S., and Chen, J.: Action currents of the single lateral-line nerve fiber of fish. I. On the spontaneous discharge. *Japanese J. Physiol.* 1:87, 1950.
- ¹⁴³ —: Action current of the single lateral-line nerve fiber of fish. II. On the discharge due to stimulation. *Japanese J. Physiol.* 1:179, 1951.
- ¹⁴⁴ —: Neural mechanisms of the lateral-line organ of fish (fundamental neural mechanism of sensory organs in general). *Japanese J. Physiol.* 1:264, 1951.
- ¹⁴⁵ Katz, B. and Kuffler, S. W.: Excitation of the nerve-muscle system in crustacea. *Proc. Roy. Soc. London, s.B.* 133:374, 1946.
- ¹⁴⁶ a. Keynes, R. D.: The leakage of radioactive potassium from stimulated nerve. *J. Physiol.* 113:99, 1951.
- b. —: The ionic movements during nervous activity. *J. Physiol.* 114:119, 1951.
- ¹⁴⁷ — and Lewis, P. R.: The resting exchange of radioactive potassium in crab nerve. *J. Physiol.* 113:73, 1951.
- ¹⁴⁸ — and Lewis, P. R.: The sodium and potassium content of cephalopod nerve fibres. *J. Physiol.* 114:151, 1951.
- ¹⁴⁹ Kirschner, L. B. and Stone, W. E.: Action of inhibitors at the myoneural junction. *J. Gen. Physiol.* 34:821, 1951.

- 150 Kirstein, L.: Early effects of oxygen lack and carbon dioxide excess on spinal reflexes. *Acta physiol. Scandinav.* 23: Suppl. 10, 1951.
- 151 Korey, S. R.: Effect of dilantin and mesantoin on the giant axon of the squid. *Proc. Soc. Exp. Biol. & Med.* 76:297, 1951.
- 152 Koshtoyantz, K. S.: Enzymatic-chemical hypothesis of nerve action. 18th Internat. Physiol. Congress, 1950, p. 311.
- 153 Kuffler, S. W.: Transmission processes at nerve-muscle junctions. In Barron (ed.) *Modern Trends in Physiology and Biochemistry*. New York, Academic Press, 1952, p. 277.
- 154 —: Transmitter mechanism at the nerve-muscle junction. *Arch. Sc. Physiol.* 3:585, 1949.
- 155 — and Katz, B.: Inhibition at the nerve-muscle junction in crustacei. *J. Neurophysiol.* 9:337, 1941.
- 156 —, Hunt, C. C. and Quilliam, J. P.: Function of medullated small-nerve fibers in mammalian ventral roots: efferent muscle spindle innervation. *J. Neurophysiol.* 14:29, 1951.
- 157 Kugelberg, E. and Cobb, W.: Repetitive discharges in human motor nerve fibers during the post-ischaemic state. *J. Neurol. Neurosurg. & Psychiat.* 14:88, 1951.
- 158 Laget, P., Lavigne, S., and Gaillard, R.: Contribution a l'étude électrophysiologique de l'anoxie du nerf de mammifère. *Compt. rend. Soc. de biol.* 144:1602, 1950.
- 159 — and Legoux, J. P.: Contribution a l'étude de la chémoception de l'anhydride carbonique. *Acta physiol. Scandinav.* 22:47, 1951.
- 160 —, Vianna, U., Lavigne, S.: Effets protecteur de l'anhydride carbonique vis a vis de la dépolarization anoxique des racines rachidiens de Mammifères. *Compt. rend. Soc. de biol.* 145:629, 1951.
- 161 Lambert, E. H., Treanor, W. J., and Herrick, J. F.: Effect of heat and ultrasound on conduction in bullfrog nerve. *Federation Proc.* 10:78, 1951.
- 162 Laporte, Y.: Continuous conduction of impulses in peripheral myelinated nerve fibers. *J. Gen. Physiol.* 35:343, 1951.
- 163 — and Lloyd, D. P. C.: Disynaptic reflex linkage between muscles of a myotatic unit. *Federation Proc.* 10:78, 1951.
- 164 Larrabee, M. G., Edwards, C. and Garcia-Ramos, J.: Glucose requirements of sympathetic ganglia. *Federation Proc.* 10:79, 1951.
- 165 LeFevre, P. G.: Excitation characteristics of the squid giant axon: A test of excitation theory in a case of rapid accommodation. *J. Gen. Physiol.* 34:19, 1950.
- 166 Legoux, S. P. and Thieulin, R.: L'inhibition anélectrotonique test sensible de l'état physiologique de la fibre nerveuse; son emploi a l'étude de l'action du CO₂. *Compt. rend. Soc. de biol.* 145:251, 1951.
- 167 —: L'inhibition anélectrotonique. *Compt. rend. Soc. de biol.* 145:548, 1951.
- 168 —: L'inhibition anélectrotonique, test sensible de l'état physiologique des fibres nerveuses. Application a l'étude des modification produites par les variations de température. *Compt. rend. Soc. de biol.* 145:975, 1951.
- 169 Liu, Y. M.: Does iodacetamide delay the anoxic depolarization of frog nerve? *Chinese J. Physiol.* 17:225, 1950.
- 170 Lloyd, D. P. C.: Electrical signs of impulse conduction in spinal motoneurons. *J. Gen. Physiol.* 35:255, 1951.
- 171 —: After-currents, after-potentials, excitability and ventral root electrotonics in spinal motoneurons. *J. Gen. Physiol.* 35:289, 1951.
- 172 Lorente de N6, R.: A Study of Nerve Physiology, Part I. Studies from the Rockefeller Institute for Med. Research, vol. 131, 1947.

- 173 —: A Study of Nerve Physiology, Part II. Studies from the Rockefeller Institute for Med. Research, vol. 132, 1947.
- 174 —: On the effect of certain quaternary ammonium ions upon frog nerve. *J. Cell. Comp. Physiol.* 33: Suppl. 1, 1949.
- 175 —: The ineffectiveness of the connective tissue sheath of nerve as a diffusion barrier. *J. Cell & Comp. Physiol.* 35:195, 1950.
- 176 —: Equilibrium of frog nerve with different external concentrations of sodium ions. *J. Gen. Physiol.* 35:145, 1951.
- 177 —: On the existence of a gradient of sensitivity to the lack of sodium in the spinal roots of the bullfrog. *J. Gen. Physiol.* 35:183, 1951.
- 178 —: On the effect of cocaine upon sodium deficient frog nerve. *J. Gen. Physiol.* 35:203, 1951.
- 179 Lowenstein, O. and Roberts, T. D. M.: The localization and analysis of the responses to vibration from the isolated elasmobranch labyrinth. A contribution to the problem of the evolution of hearing in vertebrate. *J. Physiol.* 114:471, 1951.
- 180 Lubinska, L.: Nerve regeneration at different temperatures. 18th Internat. Physiol. Congress, 1950, p. 343.
- 181 Lundberg, A.: On the effect of temperature on the depolarization of frog nerve fibers. *Acta physiol. Scandinav.* 22:348, 1951.
- 182 —: On the ability of some cations to inhibit the potassium depolarization of frog nerve fibers. *Acta physiol. Scandinav.* 22:365, 1951.
- 183 —: Electrotonus in frog spinal roots and sciatic trunk. *Acta physiol. Scandinav.* 23:234, 1951.
- 184 —: Differential effect of K^+ and Rb^+ ions on frog nerve fiber. *Acta physiol. Scandinav.* 23:263, 1951.
- 185 —: Differences in after potentials of frog motor and sensory A fibers. *Acta physiol. Scandinav.* 23:279, 1951.
- 186 Lussier, J. J. and Rushton, W. A. H.: The relation between the space constant and conduction velocity in nerve fibers of the A group from the frog's sciatic. *J. Physiol.* 114:399, 1951.
- 187 —: Excitability of the nodes of Ranvier in a nerve trunk. *J. Physiol.* 115:53P, 1951.
- 188 Malcolm, D. S.: A method of measuring reflex times applied in sciatic and other conditions due to nerve-root compression. *J. Neurol., Neurosurg. & Psychiat.* 14:15, 1951.
- 189 Marmont, G.: Studies on the axon membrane. I. A new method. *J. Cell & Comp. Physiol.* 34:351, 1949.
- 190 Monnier, A. M.: Les bases physico-chimiques de l'action du calcium sur l'activité nerveuse. *Arch. Sc. Physiol.* 3:177, 1949.
- 191 —: Le facteur d'amortissement des processus d'excitation. Sa mesure. Sa signification fonctionnelle. *Arch. Sc. Physiol.* 3:371, 1949.
- 192 —: The damping factor of neuron excitation processes and its correlates with the ionic environment. 18th Internat. Physiol. Congress, 1950, p. 367.
- 193 Nachmansohn, D. (ed.): First Conference on the Nerve Impulse. New York, Josiah Macy Jr. Foundation, 1950.
- 194 — (ed.): Second Conference on the Nerve Impulse. New York, Josiah Macy, Jr. Foundation, 1951.
- 195 —: Chemical mechanisms of nerve activity. In Barron (ed.) *Modern Trends in Physiology and Biochemistry*. New York, Academic Press, 1952.
- 196 —: Energy sources of bioelectricity. In McElroy and Glass (eds.) *Phosphorus Metabolism*. Baltimore, Johns Hopkins Univ. Press, 1951.

- 197 — and Wilson, I. B.: The enzymic hydrolysis and synthesis of acetylcholine. *Advances Enzymol.* 12:259, 1951.
- 198 Nastuk, W. L.: The electrical activity of single muscle fibers at the neuromuscular junction. 18th Internat. Physiol. Congress, 1950, p. 373.
- 199 —: Membrane potential changes at a single muscle end plate produced by acetylcholine. *Federation Proc.* 10:96, 1951.
- 200 — and Hodgkin, A. L.: The electrical activity of single muscle fibres. *J. Cell & Comp. Physiol.* 35:39, 1950.
- 201 Nicol, J. A. C.: Giant axons and synergic contractions in *Branchiomma vesiculosum*. *J. Exper. Biol.* 28:22, 1951.
- 202 Opatowski, I.: The velocity of conduction in nerve fiber and its electric characteristics. *Bull. Math. & Biophys.* 12:277, 1950.
- 203 Orsini, D., Laget, P., and Lavigne, S.: Sur les propriétés électrophysiologique des nerfs d'oiseaux. *Compt. rend. Soc. de biol.* 145:1073, 1951.
- 204 Parpart, A. K. and Ballentine, R.: Molecular anatomy of the red cell plasma membrane. In Barron (ed.) *Modern Trends in Physiology and Biochemistry*. New York, Academic Press, 1952.
- 205 Pinelli, P. and Buchthal, F.: Duration, amplitude and shape of muscle action potentials in poliomyelites. *EEG Clin. Neurophysiol.* 3:497, 1951.
- 206 Posternak, J. and Mangold, R.: Action des narcotiques sur les fibres nerveuses. 18th Internat. Physiol. Congress, 1950, p. 397.
- 207 Prosser, C. L. (ed.): *Comparative Animal Physiology*. Philadelphia, Saunders, 1950.
- 208 —: Problems in the comparative physiology of nervous systems. In Barron (ed.) *Modern Trends in Physiology and Biochemistry*. New York, Academic Press, 1952.
- 209 —, Curtis, H. J., and Travis, D. M.: Action potentials from some invertebrate non-striated muscles. *J. Cell & Comp. Physiol.* 38:299, 1951.
- 210 Puckett, W. O., Grundfest, H., McElroy, W. D., and McMillen, J. H.: Damage to peripheral nerves by high velocity missiles without a direct hit. *J. Neurosurg.* 3:294, 1946.
- 211 Pumphrey, R. J. and Young, J. Z.: The rates of conduction of nerve fibres of various diameters in Cephalopods. *J. Exper. Biol.* 15:453, 1938.
- 212 Rashbass, C. and Rushton, W. A. H.: The relation of structure to the spread of excitation in the frog's sciatic trunk. *J. Physiol.* 110:110, 1949.
- 213 Rexed, B. and v. Euler, U. S.: The presence of histamine and noradrenalin in nerve as related to their content of myelinated and unmyelinated fibres. *Acta psychiat. et neurol.* 26:61, 1951.
- 214 — and Rexed, U.: Degeneration and regeneration of corneal nerves. *Brit. J. Ophthalm.* 35:38, 1951.
- 215 Richards, R. L.: Ischaemic lesions of peripheral nerves; a review. *J. Neurol., Neurosurg. & Psychiat.* 14:76, 1951.
- 216 de Roeth, A., Jr.: Role of acetylcholine in nerve activity. *J. Neurophysiol.* 14:55, 1951.
- 217 Rosenblueth, A. and Garcia-Ramos, J.: The local responses of mammalian spinal roots to alternating sinusoidal currents. *J. Cell & Comp. Physiol.* 38:321, 1951.
- 218 — and Luco, J. V.: The local responses of myelinated mammalian axons. *J. Cell. & Comp. Physiol.* 36:289, 1950.
- 219 —, Wiener, A., Pitts, N., and Garcia-Ramos, J.: An account of the spike potential of axons. *J. Cell. & Comp. Physiol.* 32:275, 1948.

- ²²⁰ Rothenberg, M. A.: Studies on permeability in relation to nerve function. II. Ionic movements across axonal membrane. *Biochim. et Biophys. Acta*, 4:96 1950.
- ²²¹ Rothstein, A. and Meier, R.: The relationship of the cell surface to metabolism. *J. Cell. & Comp. Physiol.* 38:245, 1951.
- ²²² Rushton, W. A. H.: A theory of the effects of fibre size in medullated nerve. *J. Physiol.* 115:101, 1951.
- ²²³ Sandow, A. and Mandel, H.: Effects of potassium and rubidium on the resting potential of muscle. *J. Cell & Comp. Physiol.* 38:271, 1951.
- ²²⁴ Sato, M., Nadao, M., Terauchi, C., Yamanaka, T., and Matsumoto, M.: The accommodation curve of nerve and nerve fiber, with special reference to the "breakdown of accommodation", and the effects of veratrine, guanidine and aconitine upon these. *Japanese J. Physiol.* 1:255, 1951.
- ²²⁵ —: Comparative measurements of accommodation in two nerve fibers of different sizes. *Japanese J. Physiol.* 1:309, 1951.
- ²²⁶ Scherrer, J.: Action de la strychnine sur le réflexe segmentaire spinal. *Compt. rend. Soc. de biol.* 145:1031, 1951.
- ²²⁷ Schneider, D.: Die lokale reizung und blockierung im internodium der isolierten markhaltigen nervenfaser des frosches. *Ztschr. Verg. Physiol.* 32:34, 1950.
- ²²⁸ Schoepfle, G. M.: Electrotonic potentials elicited by threshold stimuli from sheath-free nerves at different temperatures. *Am. J. Physiol.* 163:229, 1950.
- ²²⁹ — and Erlanger, J.: Further observations on local responses of single medullated fibers in frog's phalangeal nerve. *Federation Proc.* 10:120, 1951.
- ²³⁰ Schriever, H.: Untersuchungen zur potential entstehung im nerven. 18th Internat. Physiol. Congress, 1950, p. 439.
- ²³¹ Scott, D., Jr.: Response of Pacinian corpuscles to oscillatory stimulation. *Federation Proc.* 10:123, 1951.
- ²³² Seaman, G. R. and Houlihan, R. K.: Enzyme systems in *Tetrahymena geleii* S. II. Acetylcholine esterase activity. Its relation to mobility of the organism and to coordinated ciliary action in general. *J. Cell & Comp. Physiol.* 37:309, 1951.
- ²³³ Shanes, A. M.: Potassium movements and nerve activity. *Federation Proc.* 10:124, 1951.
- ²³⁴ —: Factors in nerve functioning. *Federation Proc.* 10:611, 1951.
- ²³⁵ —: Potassium movement in relation to nerve activity. *J. Gen. Physiol.* 34:795, 1951.
- ²³⁶ —: Electrical phenomena in nerve. III. Frog sciatic nerve. *J. Cell. & Comp. Physiol.* 38:17, 1951.
- ²³⁷ Shedlovsky, T.: Protochemical cells. *Science.* 113:561, 1951.
- ²³⁸ Sinclair, D. C. and Hinshaw, J. R.: A comparison of the sensory disassociation produced by procaine and by limb compression. *Brain.* 73:480, 1950.
- ²³⁹ —: Sensory changes in nerve blocks induced by cold. *Brain.* 74:318, 1951.
- ²⁴⁰ Skouby, A. P.: Sensitization of pain receptors by cholinergics substances. *Acta physiol. Scandinav.* 24:174, 1951.
- ²⁴¹ Stämpfli, R. and Zotterman, Y.: Nachweis der saltatorischen erregungsleitung an intakten nervenstam. *Helvet. Physiol. acta.* 9:208, 1951.
- ²⁴² Steinbach, H. B.: Ion binding in muscle homogenates. *Am. J. Physiol.* 163:236, 1950.
- ²⁴³ —: Ionic problems. *Trans. 2nd Conf. on Nerve Impulse.* New York, Josiah Macy, Jr., Foundation, 1951.
- ²⁴⁴ —: Permeability. *Ann. Rev. Physiol.* 13:21, 1951.

- 245 —: The sodium and potassium balance of muscle and nerve. In Barron (ed.) *Modern Trends in Physiology and Biochemistry*. New York, Academic Press, 1952.
- 246 Strohl, A.: Variations de la résistance apparente de la membrane de la fibre nerveuse suivant le sens de passage, l'intensité et la durée d'un courant continu. *J. Physiol.* 43:55, 1951.
- 247 Ström, G.: Physiological significance of post-tetanic potentials of the spinal monosynaptic reflex. *Acta physiol. Scandinav.* 24:61, 1951.
- 248 Suckling, E. E. and Suckling, J. A.: The electrical response of the lateral line system of fish to tone and other stimuli. *J. Gen. Physiol.* 34:1, 1950.
- 249 Sum Suden, C. and Marazzi, A. S.: Synaptic inhibitory action of adrenalin at parasympathetic synapses. *Federation Proc.* 10:138, 1951.^o
- 250 Sunderland, S.: Regeneration phenomena in human peripheral nerves. In Weiss, P. (ed.) *Genetic Neurology*. Chicago, University of Chicago Press, 1950.
- 251 —: The function of nerve fibers whose structure has been disorganized. *Anat. Rec.* 109:503, 1951.
- 252 Svaetichin, G.: A combination of microscopes and micromanipulators for electrophysiological investigations on single nerve cells. *Acta physiol. Scandinav. Suppl.* 86, 24:15, 1951.
- 253 —: Low resistance micro-electrodes. *Acta physiol. Scandinav. Suppl.* 86, 24:5, 1951.
- 254 —: Analysis of action potentials from single spinal ganglion cells. *Acta physiol. Scandinav. Suppl.* 86, 24:23, 1951.
- 255 Tasaki, I.: Excitation of single nerve fiber by action current from another single fiber. *J. Neurophysiol.* 13:177, 1950.
- 256 —: The threshold conditions in electrical excitation of the nerve fiber. Part I. *Cytologia.* 15:205, 1950.
- 257 —: The threshold conditions in electrical excitation of the nerve fiber. Part II. *Cytologia.* 15:219, 1950.
- 258 —: Nature of the local excitatory state in the nerve fiber. *Japanese J. Physiol.* 1:75, 1950.
- 259 —: Electrical excitation of the nerve fiber. I. Excitation by linearly increasing currents. *Japanese J. Physiol.* 1:1, 1950.
- 260 — and Sakaguchi, M.: Electrical excitation of the nerve fiber. II. Excitation by exponentially increasing currents. *Japanese J. Physiol.* 1:7, 1950.
- 261 — and Sato, M.: On the relation of the strength-frequency curve in excitation by alternating current to the strength-duration and latent addition curves of the nerve fiber. *J. Gen. Physiol.* 34:373, 1951.
- 262 — and Ushiyama, J.: Über den Effekt von Saponin und einigen anderen Chemikalien auf die erregungsleitung der einzelnen markhaltigen Nervenfasern. *Helvet. physiol. acta.* 8:77, 1950.
- 263 Thomas, P. K. and Young, J. Z.: Internode lengths in the nerves of fishes. *J. Anat.* 83:336, 1949.
- 264 Tobias, C. A. and Dunn, R. W.: Analysis of microcomposition of biological tissue by means of induced radioactivity. *Science.* 109:109, 1949.
- 265 Tobias, J. M.: On ultrastructure and function in nerve. Nonelectrical, physical aspects of excitation and conduction, as deduced primarily from polarization experiments. In Barron (ed.) *Modern Trends in Physiology and Biochemistry*. New York, Academic Press, 1952.
- 266 Toman, J. E. P., Woodbury, J. W., and Woodbury, L. A.: Mechanism of nerve

- conduction block produced by anticholinesterases. *J. Neurophysiol.* 10:429, 1947.
- ²⁶⁷ Turner, R. S.: Functional anatomy of the giant fiber system of *Calinassa californiensis*. *Physiol. Zool.* 23:35, 1950.
- ²⁶⁸ Ussing, H. H.: Active transport and diffusion of ions through living membranes. 18th Internat. Physiol. Congress, 1950. Mimeographed unclassified Technical Report, ONRL 101-50. American Embassy, London.
- ²⁶⁹ — and Zerahn, K.: Active transport of Na^+ as the source of electric current in the short circuited isolated frog skin. *Acta physiol. Scandinav.* 23:110, 1951.
- ²⁷⁰ Van Harreveld, A.: Spontaneous reinnervation of paretic muscle. 18th Internat. Physiol. Congress, 1950, p. 246.
- ²⁷¹ —: The potassium permeability of the myelin sheath of a vertebrate nerve. *J. Cell. & Comp. Physiol.* 35:331, 1950.
- ²⁷² —: Asphyxial potassium loss of mammalian nerve. *J. Cell & Comp. Physiol.* 38:199, 1951.
- ²⁷³ —, Foster, R. J. and Fasman, G. D.: Effect of diphenyl hydantoin (dilantin) on ether and pentobarbital (nembutal) narcosis. *Am. J. Physiol.* 166:718, 1951.
- ²⁷⁴ Wagner, H. G., Hartline, H. K., and Wagan, I. H.: Subliminal excitation and refractoriness in single photoreceptor elements. *Federation Proc.* 10:141, 1951.
- ²⁷⁵ Wall, P. D. and Horwitz, N. H.: Observations on the physiological action of strychnine. *J. Neurophysiol.* 14:257, 1951.
- ²⁷⁶ Weidmann, H.: Some properties of vagal stretch receptors. 18th Internat. Physiol. Congress, 1950, p. 507.
- ²⁷⁷ Weidmann, S.: Electrical characteristics of Sepia axons. *J. Physiol.* 114:373, 1951.
- ²⁷⁸ —: Membraorderstand in verlauf der herzaktions. *Helvet. physiol. acta.* 9:C40 1951.
- ²⁷⁹ —: Effect of current flow on the membrane potential of cardiac muscle. *J. Physiol.* 115:227, 1951.
- ²⁸⁰ Welsh, J. H. and Maynard, D. M., Jr.: Electrical activity of a single ganglion. *Federation Proc.* 10:145, 1951.
- ²⁸¹ Wiersma, C. A. G.: A bifunctional single motor axon system of a crustacean muscle. *J. Exper. Biol.* 28:13, 1951.
- ²⁸² —: On the innervation of the muscles in the leg of the lobster, *homarus vulgaris* Milne Edwards. *Arch. néerl. zool.* 8:384, 1951.
- ²⁸³ — and Turner, R. S.: The interaction between the synapses of a single motor fiber. *J. Gen. Physiol.* 34:137, 1950.
- ²⁸⁴ Woldring, S. and Dirken, M. N. J.: Site and extension of bulbar respiratory center. *J. Neurophysiol.* 14:227, 1951.
- ²⁸⁵ Woodbury, L. A., Hecht, H. H., and Christopherson, A. R.: Membrane resting and action potentials of single cardiac muscle fibers of the frog ventricle. *Am. J. Physiol.* 164:307, 1951.
- ²⁸⁶ Wyss, O. A. M.: Fibre type and frequency effect as factors determining response to afferent stimulation. *EEG Clin. Neurophysiol.* 2:453, 1950.
- ²⁸⁷ —: Éléments physiologiques de l'électroencéphalogramme. *J. Suisse Med.* 81:175, 1951.
- ²⁸⁸ — and Rivkine, A.: Les fibres afférentes du nerf vague participant aux réflexes respiratoires. *Helvet. physiol. acta.* 8:87, 1950.
- ²⁸⁹ Yahr, M. D., Herz, E., Moldaver, J., and Grundfest, H.: Electromyographic patterns in reinnervated muscle. *Arch. Neurol. & Psychiat.* 63:728, 1950.

- ²⁹⁰ Yamagiwa, K.: The interaction in various manifestations (Observations on Lillie's nerve model). Part I. The accelerating action. *Japanese J. Physiol.* 1:40, 1950.
- ²⁹¹ —: The interaction in various manifestations (Observations on Lillie's nerve model). Part II. The effects on the distance travelled and the refractory period. *Japanese J. Physiol.* 1:48, 1950.
- ²⁹² —: The electro-saltatory transmission of nervous impulse. (Model experiments and theoretical considerations). *Japanese J. Physiol.* 2:79, 1951.
- ²⁹³ —: Facilitation and inhibition, model experiments and a new hypothesis. *Japanese J. Physiol.* 1:195, 1951.
- ²⁹⁴ —: Interactive excitability in Lillie's nerve model. *Japanese J. Physiol.* 1:269 1951.
- ²⁹⁵ Young, J. Z.: The determination of the characteristics of nerve fibers. In Weiss, P. (ed.) *Genetic Neurology*. Chicago, University of Chicago Press, 1950.

Regional Physiology of the Central Nervous System

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MOTOR FUNCTIONS

SPINAL LEVEL. Regarding regional activities of the injured human spinal cord, Pollock, Boshes, Finkelman, Chor and Brown³³ have reported that the greater the number of segments in the distal end of the injured spinal cord, the greater is the potential total activity. The smaller the number of segments, the fewer are the reflex responses and the more fragmentary are the muscle group contractions. Spasticity, pluck reflexes and pseudospontaneous spasms are most frequently found with injury to the cervical and upper thoracic portions of the spinal cord. With the former there are fewer instances of change from flexor to extensor positions, which occur mostly in lower thoracic injuries. The efficacy of a distended bladder as stimulus for a pseudospontaneous spasm is less in the cervical and the upper thoracic segments than below.

Cerebellar Level. Electro-anatomic studies on the cat by Snider and Eldred⁴⁰ have established the existence of much more extensive cerebro-cerebellar connections than have hitherto been thought possible and have furnished additional data on the functions of some of these connections. Stimulation of the posterior sigmoid gyrus evokes responses in the contralateral anterior cerebellar lobe and middle and posterior folia of both paramedian lobules. Stimulation of the coronal gyrus (tactile receiving area-face) evokes responses in the contralateral lobulus simplex and anterior folia of both paramedian lobules. Stimulation of anterior sigmoid and anterior coronal gyri (leg, arm and face-motor) evokes responses in cerebellar areas identical to those described for the tactile system. Stimulation of the ectosylvian and sylvian gyri (auditory receiving area) evokes responses in tuber vermis, folium vermis and lobulus simplex. Stimulation of the lateral cerebral gyrus (visual receiving area) evokes responses in lobulus simplex, folium vermis and tuber vermis.

Diencephalon. Carpenter and Mettler⁹ have analyzed the effects of ablations of agranular cortex upon choreoid hyperkinesia produced in monkeys by means of bilateral subthalamic lesions placed by stereotaxic technics.

Subthalamic hyperkinesia was not eliminated or reduced in persistence or severity by subtotal ablation of area six contralateral to the dyskinesia. Destruction of areas four and six contralateral to the symptom eliminated subthalamic hyperkinesia and resulted in paresis without spasticity. Even profound paresis due to destruction of portions of the internal capsule in this region of the subthalamus was not found to prohibit the appearance and persistence of subthalamic hyperkinesia. The authors have presented the hypothesis that area six does not play a role in the neural mechanism responsible for subthalamic hyperkinesia in the monkey. In so far as the results of this study are applicable to man they suggest that agranular cortex ablation will relieve ballismus only to the extent that paresis is produced.

Cortical Level. In a critical review of the conventional scheme of cortical localization and the many differences revealed by various methods, Walshe⁴³ recalls that punctate electrical stimulation of the cerebral cortex is a grossly artificial mode of activating the cortex and that it does not reveal the natural plan of organization of movements in the cortex. The concept of a fixed cortical mosaic in which muscles are supposed to be represented and in which particular Betz cells are said to stand in direct relation to particular anterior horn cells and thus with particular muscles, is compatible with the possession of any integrating functions by the cortex.

The concept of diaschisis or remote effects of brain lesions implies a similar flexibility in cerebral localization. According to Riese,³⁷ in unilateral brain lesions of great momentum ipsilateral paralysis is frequent, though, as a rule, incomplete. Neither pressure nor interruption of uncrossed cortico-spinal tracts can explain the transient character, the initial or exclusive appearance of ipsilateral paralysis, and the dissociation in physiologic type between contralateral and homolateral paralysis. The symmetrical areas of the intact hemisphere are submitted to primary diaschisis or sudden arrest of nervous function which in its turn determines secondary diaschisis in lower levels of the opposite half of the body, thus, producing flaccid, ipsilateral paralysis. If the primary diaschisis in the symmetrical cerebral areas does not wear off rapidly, ipsilateral paralysis assumes the spastic type, due to the secondary release of the lower levels having regained their function.

Experimentally, the phenomenon of overlapping fields of cortical representation has been demonstrated as a factual support of a flexible concept of cerebral localization. Using single pulses, Liddell and Phillips²³ have elicited flick movements of thumb, index and minimus, of hallux and other toes and of the tongue and the angle of the mouth from large overlapping areas centered on the middle, medial and lateral thirds respectively of the

precentral gyrus. If the frequency of stimulation was increased, this simple pattern of representation dissolved into the classical motor map.

While reshaping of the classical doctrine of cerebral localization is thus in progress, contributions continue to be made to a more insular type of cerebral representation of function. The delimitation and investigation of a supplementary motor area by Penfield and Welch³¹ may be cited as an example. The supplementary motor area is situated almost altogether within the median longitudinal fissure and anterior to the primary motor foot area. The threshold for stimulation of this area is a little higher than for the precentral and post-central regions. In the monkey, experimental stimulation of the supplementary motor area has revealed a motor representation of the contralateral extremities and inhibition of spontaneous grasping in the opposite hand; removal of the area has resulted in forced or "reflex" grasping. In man the following signs have resulted from cortical stimulation: vocalization, inhibition of voluntary activity, assumption of characteristic postures and performance of complex maneuvers, pupillary dilatation, a few sensory experiences and local seizures. In general, the effects are ipsilateral as well as contralateral, the most frequent effect being contraversion and movement of the contralateral arm.

The influence of forebrain stimulation upon cortical evoked movements as well as recurrently produced knee jerks in the cat has been investigated by Hodes, Peacock and Heath,¹⁷ and Peacock and Hodes.³⁰ The pathway for unilateral inhibition is traced from a suppressor cortex via the caudate nucleus, putamen and pallidum to the nucleus ventralis anterior of the thalamus. From this nucleus, inhibitory influences are sent to the motor cortex. The pathway for bilateral inhibition involves the cingulate gyrus, septal nuclei and midline thalamic nuclei funnelling their effects into the hypothalamus. From this region descending inhibitory influences reach the medial reticular formation whence they are sent to the spinal motor neurones. Neural masses in the forebrain were uncovered, stimulation of which facilitated both reflex and cortically evoked movement. The former effect appears to originate in the diencephalon and direct its influence caudally. Exclusive effects on the latter response seem to be localized more rostrally and act by an influence in the motor cortex.

SENSORY FUNCTIONS

Spinal Level. The spontaneous complaint of burning pain is made in most cases soon after injury to the spinal cord. Pollock, Brown, Boshes, Finkelman, Chor, Arief and Finkle³⁴ feel that this pain originates from the distal end of the segment proximal to the injury of the spinal cord. The

pain is stated to be quite similar to the pains referred from a neuroma at the end of the proximal segment of an injured peripheral nerve.

Subcortical Level. The role of cortical and subcortical centers in the appreciation of various forms of sensation has been of interest to neurologists and neurophysiologists for many years. In the regional representation of pain, heat, cold and gross touch it has been held that nerve impulses subserving these sensory modalities enter consciousness at the level of the thalamus. Marshall²⁵ has recently revived the historical development of the modern view of central representation of pain. In cases of cortical wounds, he found that while small cortical wounds may^a affect pain, larger wounds often do not. He considers that pain is not represented in the cortex. However, the cortex is concerned with the appreciation of pain and the final elaboration of the sensory impulses depends upon mutual activities of the thalamus and the cortex.

It has been known for a long time that thalamic pain is likely to result from vascular but not from neoplastic lesions. Referring to his previous observations that aphasia may result from rapidly growing tumors but not from those of slow momentum involving, however, the critical area of speech, Riese³⁸ has raised the same problem for thalamic pain. In none of these cases of rapidly growing tumors of the thalamus did pain occur. The author concluded that the effect of the momentum of brain lesions differs according to the function disturbed.

In the course of an investigation of the behavioral capacities of long-surviving mesencephalic and bulbo-spinal cats, Macht²⁴ has observed that these animals will accept certain substances as food but will reject others. Mesencephalic and bulbo-spinal preparations readily swallow liver cubes dipped in a 0.9 per cent solution of sodium chloride, if the cubes are placed on the tongue. Dextrose-dipped liver cubes were never rejected by any animal regardless of the concentration of the dextrose. Cubes dipped in quinine, saline or acetic acid solutions were rejected by all animals at certain concentrations. Thresholds for rejection were determined and were found to be essentially the same as those at which the substances were rejected by normal cats. Threshold concentrations for rejection are believed to be appreciably lower than the concentration necessary for the production of pain. The authors conclude that certain discriminatory responses relating to "taste" have a subcortical localization in the cat.

Cortical Level. Using single shock stimulation of the isolated vestibular nerve, Kempinsky²⁰ has outlined the cortical receiving area of the vestibular portion of the eighth nerve in the cat. (See review in Chapter 7.) Using the evoked potential technic, Mickle and Ades²⁷ have carried out studies of the cortical projection of auditory, vestibular, proprioceptive and tactile systems in cats. Click stimulation of the auditory system evoked cortical

responses outside the usually recognized acoustic areas, appearing as a separate area over a part of the inferior portions of the anterior ectosylvian and anterior suprasylvian gyri. Electrical stimulation of the vestibular portion of the eighth nerve and certain proprioceptive and tactile stimuli yielded a contralateral field of response in the same general area. This demonstration of a polysensory projection area, responsive to auditory, vestibular, proprioceptive and tactile stimulation, and possessing the characteristics of a primary projection, suggests that it may represent a field of integration of stimuli for the maintenance of spatial orientation.

By the same technic, Robinson and Lennox³⁹ have examined the hippocampal formation, cingulate gyrus and cerebellum in relation to functional participation in afferent receiving mechanisms. Electrical potentials in response to click stimuli and stimulation of the optic and sciatic nerves were recorded from the hippocampus. Optic and acoustic responses of slightly longer latency than recorded from the hippocampus were obtained from the posterior cingulate gyrus. These experimental observations are consistent with theoretic assumptions of Papez and MacLean as to representation of various sensory modalities in the hippocampal formation.

BEHAVIOR

Subcortical Levels. Riese³⁶ has made an attempt to correlate certain behavioral mechanisms observed in the baboon with structural arrangements he discovered in the brain stem of the same species. He has described a new pathway (connexio trigemino-quadrigenialis) and stressed, though with caution, its functional significance for the characteristic defense reaction of the species studied, in which the masticatory musculature participates.

From clinical and pathologic findings in a case of bilateral symmetrical necrosis of the corpora striata, Hawke and Donohue¹⁵ have concluded that the basal ganglia represent the reservoir of instinctual drives which control the newborn child, and are the highest level of functioning in early infancy. The basal ganglia are probably responsible for the simpler emotional responses of the infant and the lower animal, and the cerebral cortex for the more calculated intellectual responses of the adult and also of the higher animal.

A much less rigid view of regional representation of emotion has been taken by Spiegel, Wycis, Freed and Orchinik.⁴¹ They have concluded that it is not possible to refer emotional reactions to a single circumscribed nucleus within the diencephalon or to its connections with the frontal lobes, but that there exists a multiple representation of this function. From a study of nine cases of impairment of consciousness it has been concluded by Thompson⁴² that bilateral thalamic and hypothalamic lesions result in impairment of consciousness to the degree of a lethargic stupor from which

the patient can be partially aroused. Either bilateral thalamic lesions alone or hypothalamic lesions alone may produce this syndrome. The depth of a stupor does not seem to depend upon the extent of involvement of these structures. Lesions of the junction of the hypothalamus and of the subthalamus with the mesencephalon result in deep coma from which no degree of recovery is possible. Both the stupor and the coma are permanent and irreversible. Logical analysis of hidden and manifest implications of the problem of the presumable site of consciousness as well as factual surgical evidences have led Meyers²⁶ to refute Dandy's theory that the cerebral "center of consciousness" is located in the anterior striatum. According to Brain,⁸ all the evidences suggest that consciousness is impaired primarily as a result of disturbances of function of the brain-stem rather than of any remote effect upon supratentorial structures. At least three neurophysiologic types of disturbances are distinguished: (1) *petit mal* dysrhythmia, possibly associated with a discharge from the medial portion of the thalamus; (2) parasomnia with the disturbance in the posterior hypothalamic regions; and (3) a lower brain-stem disorder perhaps throwing light upon syncope.

Cortical Level. The effects of surgical lesions in the frontal agranular cortex in Rhesus monkeys on the performance of box problems requiring sequential removal of a peg and lid to obtain a reward have been studied by Berman, Robinson and Pribram.⁷ The locus of the lesion in the precentral motor cortex was found to determine the locus of paresis but neither involvement of this cortex nor of other frontal agranular cortex was related to ability to perform these learned tasks, with the exception that the more anteriorly placed lesions interfered with serially sequential performance. Mass and bilaterality of the lesion were found to be significant only after a certain threshold had been exceeded and then only in affecting the duration of disability, awkwardness of performance or laterality of paralysis.

Reviewing his war experiences with brain wounds, Bay⁴ has reached conclusions almost identical with Pierre Marie's view on localization of speech. So-called motor aphasia is believed simply to be a special type of motor disorder, affecting, in this instance, speech muscles. In other words, it is a purely articulatory defect, a form of apraxia, leaving inner speech and thought undisturbed. It is always associated with right-sided hemiplegia and can be correlated with lesions of the motor area and its neighborhood, with no predilection, however, for Broca's field. The critical area is still more restricted in lasting speech defects, where it involves the inferior part of the precentral gyrus. According to Bay, the term motor aphasia should be abandoned and replaced by cortical dysarthria. In contrast, sensory aphasia is considered by the author to be a genuine aphasia, associated with lack of understanding of spoken and written language, nominal defects, disordered symbolic thinking, alexia, agraphia, acalculia and inability to

discriminate between left and right. Sensory aphasia can be correlated with a temporo-parietal area of rather considerable extension. By far the majority of clinical cases show a combination of sensory aphasia with cortical dysarthria. According to Bay,^{5, 6} the syndrome of visual agnosia can be fully explained by the disorder of neurophysiologic processes underlying perception. There is no reason for the assumption of a specific center for gnosis or visual recognition. Oppenheimer and Weissman²⁹ believe that anosognosia or the unawareness of one's own blindness is the result of diffuse cortical disease and that in these cases a "functional" localization is more appropriate than a "topographic" one. Anosognosia described by Weinstein and Kahn⁴⁴ as a manifestation of the patient's drive to be well, appearing in a new pattern of organization in the damaged brain, was observed in 22 cases of brain tumor. The tumors were situated in various parts of the brain, including the frontal, temporal and parietal lobes, the diencephalon and the posterior fossa. In all instances, the anosognosic delusion involved more than one defect. The aspects of illness which were denied included left hemiplegia, right hemiparesis, involuntary movements of the right lower extremity, blindness, loss of memory, urinary and fecal incontinence, sexual impotence, vomiting and the fact that an operation had been performed or that the patient was ill in any way. Anosognosia never occurred as a single phenomenon but was manifested as part of a generalized disturbance of behavior.

With regard to emotional sequelae, the ablation of the convexity of the prefrontal region (areas 9 and 10) has been stated by Le Beau²¹ to produce a postoperative syndrome which is more significant than that of the orbital surface (areas 11 and 13) and much more significant than that of the mesial surface (areas 24 and 32). The ablation of area 9 is likely to produce a hypomaniac syndrome while that of area 10 is not succeeded by an appreciable postoperative syndrome. It is possible that the ablation of area 12 is succeeded by a marked apathy and disordered micturition. According to Nielsen²⁸ the anterior cingulate gyri in man, as in the monkey, contains the essential cortex for expression of emotion. Undermining of area 24 bilaterally in man produces a remarkable state of complete disinterest and apathy.

Psychiatrically the syndrome caused by prefrontal lobotomy has been described as being characterized by apathy, lack of spontaneity, fatuous equanimity, absence of finer emotional response, thoughtlessness and, at times, euphoria. Although it has been denied⁴ that there are changes in intellectual functions following prefrontal lobotomy or that there are measurable non-intellectual changes, Crown,¹¹ in a recent review, states that objective studies do not support this. The author makes a plea for more sensitive psychomotor studies.

Experimental removal of the temporal lobe or the greater part of the

parieto-temporo-preoccipital region results in loss of, and retardation in, reacquiring certain habits based upon visual and somesthetic discrimination. In addition, there are effects similar to those following prefrontal ablation—deficit on the delayed and conditioned reaction problems. Chow, Blum and Blum¹⁰ have found that removal of the frontal granular cortex in monkeys subsequently to bilateral parieto-temporo-preoccipital ablations is followed by deficits in retention or relearning of some of the somesthetic discrimination problems (roughness and temperature), additional decrement on the conditioned reaction problem, deficit or failure on the delayed reaction problem, and increase in general activity.

The disorders of function which result from organic disease of that part of the human cortex which lies posterior to the fissure of Rolando have been discussed by Reinhold.³⁵ These disorders are stated to be related to the perception of stimuli concerned with vision, hearing, touch, pain, posture, vibration, stereognosis, tactile discrimination, language in all its aspects, calculation, voluntary movement, and awareness of the body, and its orientation in space and time. The hypothesis is put forward that these functions depend upon perception, and it is suggested that each dysfunction may be related to a particular aspect of disordered perception. According to Gibbs,¹⁴ the temporal lobe subserves a hierarchy of functions. These are divisible into (a) sensation, (b) perception, (c) evaluation, and (d) judgment. The middle and posterior temporal regions are concerned with (a) and (b) and the anterior temporal region with (c) and (d).

VEGETATIVE FUNCTIONS

Spinal Level. Because of the use of antibiotics and as a result of improved nursing care, many of those who sustained injuries of the spinal cord in World War II have survived. This has permitted studies of residual effects of these injuries over several years. In such patients, interruption of central excitatory or suprasegmental reflex impulses for heat production, sweating and vasoconstriction produces defects of regulation of sweat, temperature and blood pressure (Pollock, Boshes, Chor, Finkelman, Arief and Brown³²). Inhibitory impulses from higher levels also fail to reach the distal end of the injured spinal cord so that autonomic reflexes below the injury are increased. There is a greater than usual hyperpyrexia from immersion in hot water; reflex sweating produced by bladder or rectal distension, and hypertension produced by similar stimuli and by cold are excessive.

Bulbar and Diencephalon Levels. Dirken and Woldring¹² have studied spike potentials arising in the bulbar respiratory center. Three different types of response have been picked up and a distinction made between central vagal, expiratory and inspiratory activity. The same authors⁴⁵ have located two separate bulbar respiratory areas, a ventromedial inspiratory

part and a dorsolateral expiratory part. The inspiratory area is situated mainly in the reticular substance at the level of the entrance of the vagi, while the expiratory area is connected with the spinal trigeminal root laterally and has medially a course parallel to the solitary tract.

It is now a well-established fact that obesity develops in animals following destructive lesions in or around the ventromedial nucleus of the hypothalamus. This obesity has been shown to arise primarily from an increase in food intake—i.e., from a hyperphagia. Anand and Brobeck¹ have recently demonstrated a well-localized area in the lateral hypothalamus, bilateral destruction of which is followed by a complete absence of eating. Destruction of the ventromedial nuclei and their surroundings produces hyperphagia and consequent obesity only if this lateral hypothalamic area is intact. It would appear therefore that of the two "centers" the lateral area exerts the more basic control over food intake and that its activity is regulated by the medial hypothalamic structures.

Autonomic effects, particularly alterations in blood pressure and inhibition of respiration, have been observed in man and cats by Baird, Guidetti, Reyes, Wycis and Spiegel³ on stimulation of the anterior thalamic nuclei. In cats, extensive lesions of these nuclei induced a transitory state of catalepsy and a reduced reactivity to noxious stimuli.

Cortical Level. Babkin and Van Buren² have reported that electrical stimulation of the anterior composite gyrus in dogs gives chewing, salivation, respiratory inhibition, swallowing, contraction of the esophagus, relaxation of the cardia and inhibition of the pyloric antrum. From this rostral portion of the anterior sigmoid gyrus, augmentor effects on respiration and opening of the mouth and protrusion of the tongue were seen. The effects on blood pressure were variable but occasional bradycardia occurred on stimulation of the masticatory area. From the cingulate gyrus of the cat, Hess, McDonald and Livingston¹⁶ have elicited complex visceral as well as somatic motor responses. These included dilatation of the pupils, retraction of the nictitating membranes and widening of the palpebral fissures. Respiratory arrest in response to electrical stimulation of the anterior cingulate gyrus has been described by Lennox and Robinson.²²

In the course of a continuing investigation of cardiovascular responses to cerebral stimulation, Hoff, Langford, Vester, Beckner and Thomas¹⁹ have found that these responses are enhanced by strychnine applied locally to the pressor areas of the cat's frontal lobe. Blood pressure rises obtained from electrical stimulation of the anterior sigmoid gyri of the cat's cerebral cortex are greatly facilitated by local application of 2 per cent or saturated solutions of strychnine sulfate. Renal cortical ischemia associated with blood pressure rises evoked by cerebral cortical stimulation is also enhanced by local strychninization. Facilitation produced by local strychninization

was not found to be abolished by adrenalectomy. Local strychninization of a "silent" parietal area of the cerebral cortex (from which blood pressure responses cannot be evoked) yields no facilitation of responses from the pressor areas in the frontal lobes of the cortex. The authors, therefore, concluded that strychninization exerts its facilitatory effects by action upon the cortical gray matter at the site of application.

Hoff, Kell, Hastings, Sholes and Gray¹⁸ have explored the effects of electrical stimulation of the pressor regions of the cerebral cortex and of electroshock-type stimulation of the brain upon renal vasomotor function and consequent pathologic changes in the kidney and alterations in the urine. Electrical stimulation of foci on the anterior sigmoid gyri of the cerebral cortex in acute experiments on cats produced transient elevations of arterial blood pressure together with renal cortical ischemia. These and renal vasomotor effects were greatly exaggerated when the brain was stimulated through the intact cranium with the Brief Stimulus Therapy Apparatus (BST). Unilateral renal denervation essentially abolished the ischemic changes in the kidney deprived of its nerve supply. In acute experiments following 10 to 15 stimulations of the cerebral cortex directly or of the brain with the BST apparatus, there was fatty degeneration of the renal tubule cells. In animals receiving 19 or more stimulations with the BST apparatus in acute experiments, the renal tubule cells exhibited pyknosis and fragmentation of the nuclei as well as severe fatty degeneration. Following multiple stimulations of the brain with the BST apparatus in chronic experiments lasting one to six weeks, there were pathologic changes in the kidneys presenting a picture of lower nephron nephrosis. These changes are probably the result of repeated arteriolar vasoconstriction leading to tissue anoxia and alterations in capillary permeability.

In the experiments of Hoff and co-workers, the responses show no evidence of "local sign"; a unilateral cortical stimulus produces bilateral and apparently symmetrical effects. That unilateral stimulus may, however, yield autonomic responses which are bilaterally asymmetric has been indicated by studies on healthy human subjects by Elithorn, Piercy and Crosskey.¹³ These authors have examined autonomic responses to painful stimuli in the upper limbs, using skin resistance and plethysmographic technics. When the attitude of the subject can be suitably controlled so that he can be indifferent to painful stimuli, the responses are comparatively greater on the side of stimulation.

REFERENCES

- ¹ Anand, B. K. and Brobeck, J. R.: Localization of a "feeding center" in the hypothalamus of the rat. *Proc. Soc. Exper. Biol. & Med.* 77:323-324, 1951.
- ² Babkin, B. P. and Van Buren, J. M.: Mechanism and cortical representation of the feeding pattern. *Arch. Neurol. & Psychiat.* 66:1-19, 1951.

- ³ Baird, H., Guidetti, B., Reyes, V., Wycis, H. T., and Spiegel, E. A.: Stimulation and elimination of anterior thalamic nuclei in man and cat. *Federation Proc.* 10:8-9, 1951.
- ⁴ Bay, E.: Lokalisationsfragen im Lichte neuerer Erkenntnisse bei Hirnverletzen. *Deutsche Ztschr. f. Nervenhe.* 166:431-446, 1951.
- ⁵ —: Ueber den Begriff der Agnosie. *Nervenarzt.* 22:179-187, 1951.
- ⁶ —: Schlussbemerkung zur Agnosiediskussion. *Nervenarzt.* 22:309-310, 1951.
- ⁷ Berman, A. J., Robinson, F., and Pribram, K. H.: Problems concerning functions on frontal agranular cortex. *Federation Proc.* 10:13-14, 1951.
- ⁸ Brain, W. R.: The cerebral basis of consciousness. *Proc. Roy. Soc. Med.* 44:37-42, 1951.
- ⁹ Carpenter, M. B. and Mettler, F. A.: Analysis of subthalamic hyperkinesia in the monkey with special reference to ablations of agranular cortex. *J. Comp. Neurol.* 95:125-157, 1951.
- ¹⁰ Chow, K. L., Blum, J. S., and Blum, R. A.: Effects of combined destruction of frontal and posterior "associative areas" in monkeys. *J. Neurophysiol.* 14:59-71, 1951.
- ¹¹ Crown, S.: Psychological changes following prefrontal leucotomy: A review. *J. Ment. Sc.* 97:49-83, 1951.
- ¹² Dirken, M. N. J. and Woldring, S.: Unit activity in bulbar respiratory centre. *J. Neurophysiol.* 14:211-225, 1951.
- ¹³ Elithorn, A., Piercy, M. F., and Crosskey, M. A.: Local sign in autonomic responses. *J. Neurol., Neurosurg. & Psychiat.* 14:209-215, 1951.
- ¹⁴ Gibbs, F. A.: Ictal and non-ictal psychiatric disorders in temporal lobe epilepsy. *J. Nerv. & Ment. Dis.* 113:522-528, 1951.
- ¹⁵ Hawke, W. A. and Donohue, W. L.: Bilateral symmetrical necrosis of the corpora striata. *J. Nerv. & Ment. Dis.* 113:20-39, 1951.
- ¹⁶ Hess, W. R., McDonald, D. A., and Livingston, R. B.: Head-turning and eye deviation evoked by cortical excitation in the freely moving cat. *Federation Proc.* 10:63, 1951.
- ¹⁷ Hodes, R., Peacock, S. M., Jr., and Heath, R. G.: Influence of the forebrain on somato-motor activity. I. Inhibition. *J. Comp. Neurol.* 94:381-408, 1951.
- ¹⁸ Hoff, E. C., Kell, J. F., Hastings, N., Sholes, D. M., and Gray, E. H.: Vasomotor, cellular and functional changes produced in kidney by brain stimulation. *J. Neurophysiol.* 14:317-332, 1951.
- ¹⁹ Hoff, E. C., Langford, H. G., Vester, J. W., Beckner, W. W., and Thomas, P. R.: Strychnine facilitation of pressor responses evoked from cerebral cortex. *J. Neurophysiol.* 14:167-174, 1951.
- ²⁰ Kempinsky, W. H.: Cortical projection of vestibular and facial nerves in cat. *J. Neurophysiol.* 14:203-210, 1951.
- ²¹ Le Beau, J.: Sur le fonctions du lobe préfrontal. Étude du syndrome post-opératoire dans 132 topectomies et leucotomies partielles. *Rev. neurol.* 85:3-16, 1951.
- ²² Lennox, M. A. and Robinson, F.: Cingulate-cerebellar mechanisms in the physiological pathogenesis of epilepsy. *EEG Clin. Neurophysiol.* 3:197-205, 1951.
- ²³ Liddell, E. G. T. and Phillips, C. G.: Overlapping areas in the motor cortex of the baboon. *J. Physiol.* 112:392-399, 1951.
- ²⁴ Macht, M. B.: Subcortical localization of certain "taste" responses in the cat. *Federation Proc.* 10:88, 1951.
- ²⁵ Marshall, J.: Sensory disturbances in cortical wounds with special reference to pain. *J. Neurol., Neurosurg. & Psychiat.* 14:187-204, 1951.

- ²⁶ Meyers, R.: Dandy's striatal theory of "the center of consciousness." *Arch. Neurol. & Psychiat.* 65:659-671, 1951.
- ²⁷ Mickle, W. A. and Ades, H. W.: Cortical projection of postural impulses. *Federation Proc.* 10:92, 1951.
- ²⁸ Nielsen, J. M.: Anterior cingulate gyrus and corpus callosum. *Bull. Los Angeles Neurol. Soc.* 16:235-243, 1951.
- ²⁹ Oppenheimer, H. and Weissman, M.: On anosognosia. *Am. J. Psychiat.* 108:337-342, 1951.
- ³⁰ Peacock, S. M., Jr., and Hodes, R.: Influence of the forebrain on somatomotor activity. II. Facilitation. *J. Comp. Neurol.* 94:409-426, 1951.
- ³¹ Penfield, W. and Welch, K.: The supplementary motor area of the cerebral cortex. A clinical and experimental study. *Arch. Neurol. & Psychiat.* 66:289-317, 1951.
- ³² Pollock, L. J., Boshes, B., Chor, H., Finkelman, I., Arief, A. J., and Brown, M.: Defects in regulatory mechanisms of autonomic function in injuries to the spinal cord. *J. Neurophysiol.* 14:85-93, 1951.
- ³³ Pollock, L., Boshes, B., Finkelman, I., Chor, H., and Brown, M.: Spasticity, pseudospontaneous spasms, and other reflex activities late after injury to the spinal cord. *Arch. Neurol. & Psychiat.* 66:537-560, 1951.
- ³⁴ Pollock, L. J., Brown, M., Boshes, B., Finkelman, I., Chor, H., Arief, A. J., and Finkle, J. R.: Pain below the level of injury of the spinal cord. *Arch. Neurol. & Psychiat.* 65:319-322, 1951.
- ³⁵ Reinhold, M.: Some clinical aspects of human cortical function. *Brain.* 74:399-430, 1951.
- ³⁶ Riese, W.: Quelques observations sur le tronc cerebral du babouin; interpretation physiologique. *Arch. suisses de Neurol. & de Psychiat.* 66:377-379, 1950.
- ³⁷ —: Notes on ipsilateral paralysis. *Confinia neurol.* 11:98-102, 1951.
- ³⁸ —: Les tumeurs gliomateuses de la couche optique a croissance rapide et la douleur thalamique. *Rev. neurol.* 84:192-193, 1951.
- ³⁹ Robinson, F. and Lennox, M. A.: Sensory mechanisms in hippocampus, cingulate gyrus and cerebellum of the cat. *Federation Proc.* 10:110-111, 1951.
- ⁴⁰ Snider, R. and Eldred, E.: Electro-anatomical studies on cerebro-cerebellar connections in the cat. *J. Comp. Neurol.* 95:1-16, 1951.
- ⁴¹ Spiegel, E. A., Wycis, H. T., Freed, H., and Orchinik, C.: The central mechanisms of the emotions. *Am. J. Psychiat.* 108:426-431, 1951.
- ⁴² Thompson, G. N.: Cerebral area essential to consciousness. *Bull. Los Angeles Neurol. Soc.* 16:311-324, 1951.
- ⁴³ Walshe, F. M. R.: On the interpretation of experimental studies of cortical motor function: with special reference to the "operational view" of experimental procedures. *Brain.* 74:249-266, 1951.
- ⁴⁴ Weinstein, E. A. and Kahn, R. L.: The syndrome of anosognosia. *Arch. Neurol. & Psychiat.* 64:772-791, 1950.
- ⁴⁵ Woldring, S. and Dirken, M. N. J.: Site and extension of bulbar respiratory centre. *J. Neurophysiol.* 14:227-241, 1951.

Neuropathology

By A. FERRARO, M.D. AND L. ROIZIN, M.D.

INFLAMMATORY PROCESSES. Furtado and Marques¹⁶ reported that tuberculosis of the nervous system is very common in Portugal. In the authors' series of tumors of the cerebrum (number of cases not mentioned) 20 per cent were tuberculomata (Cushing noted only 4 per cent). Fifty per cent of them were situated in the posterior fossa. Tuberculomas were often multiple.

Two cases of Torulosis with the clinical course and the early objective findings consistent with the diagnosis of posterior fossa tumor and chronic productive meningitis were reported by Globus and co-workers.¹⁸ The histopathologic characteristic lesions consisted of multiple, grayish, gelatinous cysts in the brain substance. The exudate elsewhere was also characteristically gray and gelatinous. As a rule, there was little or no reaction in the brain tissue surrounding the distended perivascular spaces. Microscopic studies disclosed the organism in large numbers, dispersed in mononuclear exudate. The absence of glial reaction was striking. Giant cells were often encountered in the meningeal exudate.

An extensive granuloma of the cervical spinal cord in an eight-year old child was reported by Ley et al.²⁸ The symptoms were those of compression of the spinal cord. The granuloma was removed surgically and the child, who had a severe quadriplegia before operation, recovered completely. A study of the surgical specimen indicated that the exudative organism was the *Torula Histolytica*. Relatively often binucleate or trinucleate ganglion cells were found. Of interest is also the case reported by the same authors of a boy aged 16, in whom an acute lethargic encephalitis appeared first as an epileptic attack, followed by tic-like twitchings accompanied by occasional crying spells. This was shortly followed by death in intense hyperpyrexia. Histologically, severe inflammatory changes were found in both the white and the gray matter of the brain.

The study of Horstman²³ on the neuropathology of Teschen disease (virus encephalomyelitis of swine) revealed it to be a diffuse encephalomyelitis with characteristic lesions both as to type and distribution. The lesions were with minor exceptions confined to the gray matter in the

brain and spinal cord. Their widespread distribution in the central nervous system and particularly their striking density in the cerebellum served to distinguish Teschen disease from poliomyelitis although spinal cord lesions may be similar in both diseases.

The pathology of experimental congenital toxoplasmosis has been studied by Cowen and Wolf⁶ in young mice. The animals became infected by way of the placenta (following exposure of the mother to toxoplasma by the vaginal route during pregnancy). Lesions of toxoplasmosis in the offspring first appeared on the 9th postnatal day and later. The central nervous system was almost invariably affected, the lungs only slightly less often, and the heart and other tissues inconsistently or not at all. Large zones of inflammation, necrosis, and calcification in the brain, associated with Toxoplasmas, duplicated features typical of the human disease.

Cardona,⁴ in a review of the histologic problem of encephalitis, tried to subdivide the inflammatory process into perivascular and parenchymatous types. Among the first he considered parainfective encephalitis of Bogaert, Brain, Hunter and Turnbull (characterized by perivascular hemorrhage, edema, demyelination, etc.). He emphasized that the name of parainfection should be reserved only to the following conditions: (1) the secondary leukoencephalitis which appears generally during the convalescence of infectious diseases (especially exanthematous); (2) primitive, isolated leukoencephalitis, especially hemorrhagic, always perivascular in origin. To this group belong the old hemorrhagic encephalitis of Strümpell and Lichtenstein and the new acute hemorrhagic encephalitis of Weston Hurst (which the author feels does not differ from the hemorrhagic encephalitis of Margolis, Soloviev, Schulbaze; nor from the necrotizing hemorrhagic encephalopathy of Adams, Cammermyer, Dercums, Brown). In the latter group should also be included the subacute necrotic myelitis of Foix and Alajouanine and the various acute disseminated encephalomyelitis.

To the "parenchymatous diffuse encephalitis" belong the following diseases: the virus encephalitis (some of which are called panencephalitis) which predominantly involve the gray matter. The representative types of this condition would be: von Economo, Heine-Medin, zona diseases, Japanese and St. Louis encephalitis, the various Italian panencephalitides (Bini) rabies, exanthematous typhus, nodular encephalitis of Pette and Doering, the Inclusion encephalitis of Dawson. In addition to this type of histologic reaction, belong at times other varieties not of virus origin but of different nature such as Acroдинia, tetanus, diphtheria, typhus and even general paresis.

In a study on the effects of streptomycin upon tuberculosis of the nervous system and the meninges in guinea pigs, Luzzatto³⁰ felt that the effect of the antibiotic depends upon the evolution of the disease, duration of

therapy, and the dosage used, and is, therefore, possibly due to a different degree of the bacteriostatic action exercised by the antibiotic itself.

Allergic Processes. Ferraro and Roizin¹² reported the production of encephalomyelitis in guinea-pigs with a calcium acetate compound extracted from the brain tissue, (prepared with Bell, Hubell et al. procedure). Histologic studies disclosed circumscribed or diffuse (to a lesser extent) inflammatory reactions involving the meninges and the parenchyma at various levels of the central nervous system. Frequently, plasma cells appeared mixed with the various elements of the exudate. The process of demyelination was rather light and most perivascular in location. Both the clinical and neuropathologic findings were essentially similar to those previously reported in allergic encephalomyelitis in which the whole brain plus Freund's adjuvants was used as antigen.

Hyde and Campbell²⁴ postulated that the early plasma cell formation induced by the infective viruses gave some support to the hypothesis that the plasmacytosis in neurotropic virus disease is a primary pathologic response. They also noticed that the early stages of inflammation brought about by the injection of minute quantities of infective vaccinia and herpes virus into the skin and brain of rabbits differ in severity of the inflammation, in the amount of perivascular cuffing, and in the conspicuous early plasmacytosis, from the inflammatory picture produced by noninfective control material.

Latimer and co-workers²⁷ described two cases of neuromyolytic accident following administration of rabies vaccine. In both cases there was a history of previous antirabies treatment. In case 1, the condition was myelitic in type, with the appearance of thoracic transverse myelitis after the tenth inoculation and subsequent recovery. In case 2, it was encephalitic in character, with a systemic reaction following the first injection and the development of encephalomyelitis after the eighth inoculation, and terminating in death within 24 hours.

In view of the fact that during the recent years several investigators observed that pituitary (ACTH) and adreno-cortical hormones (ACE, Cortisone, etc.) inhibit some allergic reactions, Moyer, Jervis, and co-workers (ACTH),³³ Kabat, Wolf, and Bezer (Cortisone),²⁶ Ferraro and Roizin¹¹ (Cortone acetate Merk) have used these hormones in various animals to prevent experimental allergic encephalomyelitis. Although some discrepancies of the various investigators may be due to several factors (difference in the use of various chemical preparations, dosage and duration of experimental procedure, species, etc.) there is the general impression that parenteral administration of the above mentioned substances inhibits, at least partially, the inflammatory reaction at the site of injection and delays the encephalomyelitic process. Conversely, Wolf and co-work-

ers⁴⁹ reported the effect of Cortisone, activating Trypanosomal encephalitis and myocarditis in Rhesus monkeys.

Cazzullo and Allegranza⁵ induced an allergic experimental encephalomyelitis in guinea pigs by intramuscular and intraperitoneal injections of homologous and heterologous (human) brain emulsions plus adjuvants according to Freund's method.

Demyelinating Processes. A case of subacute ascending transverse myelitis, at first spastic and later flaccid and atrophic, was described by Gereb.¹⁷ Anatomic investigation showed three separate lesions, a total necrosis of the lower half of the spinal cord, a central glia nodule in the upper dorsal region and several foci of demyelination in the brain stem.

In a study of the "classification of diffuse demyelinating sclerosis on the basis of histopathogenesis" Greenfield¹⁹ has postulated the following forms: (1) the inflammatory reactive type of Einarson and Neel (familial and non-familial); (2) the metachromatic type (familial and non-familial) including a late infantile described by the author in 1933; and (3) the epithelioid form (familial), probably due to a general disorder of lipid metabolism.

Vogel⁴⁸ emphasized the significance of widespread acute demyelination of the gray and white matter of the brain and focal lesions of the myocardium, the adrenals, and an ovary in acute hemorrhagic pancreatitis, suggesting the possibility that the demyelination and the visceral lesions might have been caused by excessive amounts of enzymes liberated from the damaged pancreas.

The relations as well as the clinical and anatomic difference between subacute sclerosing leukoencephalitis (van Bogaert), nodular encephalitis (Pette and Doering) and encephalitis with cellular inclusions (Dawson) were discussed by Flores et al.¹⁸ in an 11-year-old girl who showed psychic disturbances, papilledoema, extrapyramidal hyperkinesia, apraxia, agraphia, and ultimate decerebrate position.

Degenerative Processes. Four cases of subacute cortical cerebellar degeneration, three of which associated with carcinoma, were described by Brain, Daniel and Greenfield.² In these cases there was also degeneration of the long tracts of the spinal cord: direct spino-cerebellar in all, pyramidal in one, and dorsal columns in the other two. In the absence of an hereditary factor in their etiology, the authors believe that the process of "abiotrophy" and special vulnerability of the Purkinje cells and nucleus dentatus probably determined the site of affection.

In postmortem examination of a member of a family presenting "hereditary perforating ulcer of the foot," Denny-Brown⁹ observed a primary degeneration of dorsal root ganglia. In addition, deposits of amyloid were found in the most severely affected ganglia. The disorder was inherited as a

simple Mendelian dominant. This disease has, however, a sporadic and familial form as well.

Sites of mineralization in the body have been investigated by Bunting³ with methods for calcium, iron, carbonate, and phosphate. Blood vessel walls in the brain and elsewhere and granular deposits in the brain, the choroid plexus, the kidney, and in other organs have all been found to contain calcium, iron, carbonate, and phosphate.

Two pathologically verified cases of Hallervorden-Spatz disease were described by Netsky, Shapiro and Zimmerman.³⁶ In one, the clinical syndrome of dystonia musculorum deformans and Friedreich's ataxia were present. In the other, there was no clinical evidence of neurologic disorder. The possibility that an alteration of iron metabolism is the defect present in dystonia was investigated, but their study of this syndrome disclosed no abnormal iron pigment. They concluded that dystonia is a symptom-complex which may be found in association with various pathologic changes.

Dense symmetrical calcification in the caudate, lenticular and dentate nuclei, demonstrable radiologically, was observed by Foley¹⁴ in a case with ataxia and spasticity. Conversely to other cases reported, there was no evidence of hypoparathyroidism. Both the patient's daughters, though free of neurologic symptoms, exhibited similar, though less marked, radiologic changes. Calcification was detected in three of the patient's four sons. Evidence is presented that the process may result from certain rare chronic infections, and that such infections may affect predisposed families.

The clinical and pathologic finding in a case of bilateral symmetrical necrosis of the corpora striata has been described by Hawke and Donohue.²¹ Five somewhat similar cases have also been reported and a tentative syndrome of the corpus striatum has been proposed.

Association between amaurotic idiocy and myoclonic epilepsy was illustrated by Haddenbrock²⁰ in the case of a boy who died when six years of age. Postmortem examination showed some deposits of fat only in the lungs, but the C.N.S. was severely affected. The cerebrum, the cerebellum and the brain stem were much reduced in size, the white matter of both the cerebrum and the cerebellum were sclerotic and showed diffuse gliosis. In most areas of the C.N.S. neurons were diminished in number and many of the remaining ones exhibited the typical swelling and deposit of lipoid substances. The globus pallidus and the cerebellum, including the dentate nucleus, were severely affected. Demyelination was conspicuous around and within the dentate nucleus and the superior cerebellar peduncle. "Myoclonus bodies" were found in the dentate nucleus and the substantia nigra though only in small numbers.

Den Hartog Jager²⁵ reported the following findings in a case of dystrophia

myotonica: (1) increase in the basophil cells of the hypophysis; (2) atrophy of the testis; (3) typical anomalies in the muscles; and (4) moderate secondary retrograde changes (pyknosis, shrinkage and falling out) in the motor ganglion cells of the facial nucleus and anterior horns in the cervical and thoracic cord. He feels that the marked abnormality of the hypophysis is the primary cause of the pathologic changes.

Nineteen cases of dystrophia myotonica (D.m.) and two cases of myotonia congenita (M.c.) have been studied by Gunnar Wohlfart.⁴⁶ Autopsy material was available only from one case of D.m. In five cases of M.c. six biopsy samples were studied. In the autopsied case of D.m. no histopathologic changes were observed in the spinal cord, the sympathetic chain, the peripheral nerves nor in the ventral or dorsal spinal roots. Microscopic changes in the muscles were found to be under certain conditions pathognomonic of the disease. The only constant histopathologic changes in D.m. was an inward migration of nuclei from the periphery of the muscle fibers to the center. Capillary loops and surrounding tissues were inclined to grow into the muscle fibers. In addition, the myofibrils were often destroyed and in 12 of 25 biopsied muscles numerous fibers with a thick peripheral layer of sarcoplasm were found. The striated fibrillar rings ("striated annulets," the "Ringbinden" of Heidenhein which were described by him as specific for myotonia) were rather common in 14 of 25 biopsies of this material. The histopathologic changes in M.c. consisted mainly of a general hypertrophy of the muscle fibers and slight alterations reminiscent of the changes encountered in the early stages of D.m.

In two cases of postpartum eklampsia Vortel⁴⁷ found, in the dilated brain arterioles, fibrinoid necrosis of their walls, extravasation of fibrin in the surrounding brain tissue, and in some places, migration of leukocytes; furthermore, hyalin thrombi in the cortical arterioles as well as capillaries, stasis, leukocytic thrombi in the dilated venules and petechial hemorrhages. In the surrounding tissue destruction of the axons, degenerated neurons and circumscribed edema were present. Fibrinoid necrosis of the branches of the hepatic artery was an interesting finding. In discussing pathogenesis, the author considered the hypersensitivity reaction of Arthus phenomenon variety and arteritis nodosa.

Myle and Lowenthal²⁴ described two cases of lipoma and lipolymphangioma of the face associated with a verrucose naevus of a metameric disposition, angiomas and partial and segmentary hemihypertrophy. The second case presented, in addition, neurofibrillar alterations and maldevelopments of the vertebral column of a dysraphic type. Biopsies from the second case indicated the neoplastic nature of the lesions and revealed particular naevous alterations in the skin and neurofibromatosis of the derma underlying the verrucose naevus.

The effects on the central nervous system of Rhesus monkey of the newer antimalarial drugs pentaquine, isopentaquine, primaquine, and pamaquine were studied by Schmidt and Schmidt.⁴¹ The effects of the four compounds were generally similar in that the main lesions were to be found in the dorsal motor nucleus of the vagus, supraoptic and paraventricular nuclei, and in a small group of cells associated with Meynert's commissure. Pamaquine differed from the other drugs in that it consistently induced lesions of moderate severity in the abducens, trochlear, and lateral oculomotor nuclei.

Reale and D'Argenio⁸ carried out experiments on rabbits, in order to establish the effect of malononitrile on the nervous tissue. They concluded that malononitrile, like so many other toxic substances, produced, at least as far as can be judged from the histopathologic data, a harmful toxodegenerative action rather than a stimulative one.

Circulatory Disorders. Eros¹⁰ observations on cerebral arteriosclerosis suggested that the primary changes of the arteries were mainly related to alterations in the elastic tissue. The elastic tissue changes permitted the recognition of two main types of cerebral arteriosclerosis: (1) the hyperplastic degenerative type and (2) the hypoplastic degenerative type. The first was characterized by a primary proliferation of the elastica, the second by the primary degeneration of the constitutionally hypoplastic elastica. There seem to be definite relationships between the type of blood vessel changes, the type of parenchymatous changes, and the clinical manifestations. The hyperplastic type of arteriosclerosis is conducive to softenings, the hypoplastic to hemorrhage.

Wildi⁴⁶ studied the cerebral cortex of 167 patients suffering from various psychiatric diseases. A special technic of silver impregnation was used. Of these cases, 107 were considered as cases of cerebral arteriosclerosis. In 50 per cent of the arteriosclerotic patients nests of astrocytic cells were found in the cerebral cortex and always in connection with the capillaries (mostly in the 3rd and 5th layer of the cortex). These nests were found in only 12 per cent of the non-arteriosclerotic cases. Although these astrocytic nests could be demonstrated only with a particular technic of impregnation and not with other methods, the author has excluded the possibility of artefacts.

Margolis et al.³¹ observed four cases of intracranial hematomas arising from rupture of small angiomatic malformations, along with two other lesions that did not bleed. The relationship of minute lesions of this nature to spontaneous cerebral hemorrhage of unknown etiology was suggested.

A series of 100 cases of fatal cerebral infarction with autopsy was analyzed by Hicks and Warren²² with emphasis on the pathologic physiology in the non-thrombotic cases, and compared with a similar series of cases of cerebral

hemorrhage previously reported. In 60 of the 100 cases of infarction there was no mechanical occlusion of cerebral vessels by thrombosis, embolism or arteriosclerosis. They concluded that apoplexy is an ischemic disease of the brain most often directly caused by cerebral vasospasm, less often by thrombosis, and least often by systemic circulatory failure, embolism, and arteriosclerosis.

Schizophrenia. Freeman and Williams¹⁵ observed that transorbital lobotomy produced minor lesions of the skull and dura. The cortex was usually very little traumatized. The distinctive lesions were within the white matter, the incision severing the thalamofrontal radiation just lateral to the anterior horn of the lateral ventricle, although sometimes a hemorrhagic cavity in the frontal white matter evolved into a cyst with pigmented walls. Wallerian degeneration could be traced into the frontal lobe and also through the internal capsule into the pons. Retrograde degeneration in the thalamus was milder than that seen after prefrontal lobotomy.

In a group of four biopsies and 20 selected topectomies of schizophrenic patients, (which prior to psychosurgery were treated with ECT or insulin or both) Roizin³⁸ found morphologic variability of the medium and large pyramidal cells associated with marked variations in the activity of the indophenol oxidase (cytochrome-c. oxidase), peroxidases, and the acid phosphatases. Generally, the oxidase and peroxidase reactions followed very closely the microscopic features and the distribution of Nissl bodies. The acid phosphatases appeared frequently more concentrated in the intracellular areas of more pronounced chromatolysis. Irregularity in reaction and distribution of acid phosphatases were noticed also in various neuronal degenerative changes. There were also variations in the morphology and enzyme activity in the glial elements involved in pseudoneuronophagia and neuronophagia.

Zarabashvili⁵⁰ investigated in eight cases the cerebral cortex obtained by lobectomy. Besides the well known histopathologic variations observed by various investigators, this author emphasized that the neurofibrils were more argentophil than normal and adhered to one another. The changes were progressive or regressive and they represented in his opinion the anatomic substratum of the finest functional lesions which could be shown by EEG.

The brain tissue of schizophrenics was compared by Messimy et al.³² with that ablated for treatment of intractable pain in mentally normal people. Most conspicuous findings consisted of degenerative changes in the ganglion cells (leading up to their disappearance), oligodendrogliosis and fibrillary astrocytosis; microglia was usually normal though it contained some fat. The leptomeninx in 5 of the 10 patients was increased in thickness and was adherent to the underlying cortex. These changes, in

the opinion of these authors, were not related to previous therapeutic treatment such as ECT or insulin coma.

Papez and Bateman³⁷ reported that abnormal changes in cytochemical processes in nerve cells occur as a constant feature of dementia praecox. In 70 biopsies, the metabolic disturbances were caused by inclusion bodies ("pleomorphic organism") which have been demonstrated by dark phase microscopy.

Aging Processes. Schenk⁴⁰ reported a pathologic study of Pick's disease in eight cases. In four of them the diagnosis was made during life and anatomic changes were typical of Pick's disease. In the other four cases, however, diagnosis had been doubtful. The histologic changes in the C.N.S. were those of Pick's disease accompanied by vascular alterations and circulatory disturbances. Cortical changes seemed to be independent of the vascular affections; therefore, the diagnosis of Pick's disease was maintained. He concluded that the cortical atrophies do not show the aspect of a systemic affection as formulated by Schaffer and that the disease process should be attributed to a combination of hereditary and exogenous factors.

In senile dementia Simma⁴² did not find significant changes in the thalamus apart from the occasional unimportant perivascular foci of atrophy caused by the circulatory disturbance. In Alzheimer's disease, especially in cases of moderate and greater severity, he almost always found retrograde cell atrophies of variable degree. Senile plaques and fibrillary changes were observed in the thalamus also, but not frequently. The foci of retrograde degeneration were found in the mediodorsal nucleus and anterior lateral nuclei as well as in the pulvinar and posterior lateral nuclei.

Miscellaneous Processes. Macroscopic examination of the brain of agitated melancholia, carried out by Liban et al.²⁹ in a 47-year-old man treated with E.C.T. revealed: recent thrombosis in the sinuses, the large pial veins, and some intracerebral veins. In addition extensive subdural and subarachnoid hemorrhages were observed; areas of hemorrhagic softening in both thalami and in the cerebellum and a few petechiae in the grey and white matter of the brain. Microscopic examination revealed signs of vasothrombosis of the small brain vessels, particularly in the thalami; degenerative changes in ganglion cells, (most marked in the frontoparietal region of the brain) accompanied in some areas by satellitosis and neuronophagia, and degenerative changes and "polar" arrangement of the Purkinje cells of the cerebellar cortex.

Danis and van Bogaert⁷ described a choroid^oangioma clinically silent in the course of a Sturge-Weber disease. In this case, the encephalotrigeminal angiomatosis appeared as a progressive disease. The ophthalmologic examination was normal. Anatomically, the predominantly unilateral temporo-occipital angiomatosis was complicated by cerebral peduncular con-

tralateral as well as cerebellar angiomatosis with calcification of the cerebellar cortex. The angiomatous network extended further along the optic nerve (the intracerebral portion) the optic chiasm, the preoptic nucleus, the spinal meninges and the anterior roots of the spinal cord.

Appel and van Bogaert¹ report in detail a clinico-pathologic study of "family Ameil" in which congenital and acquired spastic paraplegia co-existed. The conditions did not result from cerebral malformations, but from a spinal abiotrophic process similar to Strümpell's cases, with the difference that the pathology showed predilection for the anterior horns and the olivocerebellar system. This degeneration was associated with a proliferation of the macroglia cells, not only in the cortex, but also in the cerebral central and the cerebellar nuclei.

Using Danielli's modification of Gomori's method for the alkaline phosphatases and Moog's modification of the original Gomori method for acid phosphatase, Tolone and Ventura⁴³ aimed at establishing the morphologic aspects and the normal distribution of these enzyme systems in the nervous tissue of normal rabbits, dogs, and cats. They confirmed the distribution of the alkaline and acid phosphatases in the various elements of the nervous tissue as reported by several other investigators.

For better evaluation of the specificity of the histochemical reaction of acid phosphatases Naidoo and Pratt³⁵ applied the Altman-Gersh technic to preserve the histologic integrity of brain tissue and used three different media (glycerophosphate pH 5.3, adenosine triphosphate, pH 6.5, and adenosine monophosphate pH 6.5) for the incubation of the studied sections. They found that the main site of enzymatic phosphate liberation from glycerophosphate was in the cytoplasm of the neurons. The glial and neuronal nuclei were the main site of adenosine triphosphate cleavage, and adenosine monophosphate was split mainly in nerve fibers. These authors' findings confirmed similar observations made by Roizin in large pyramidal neurons of human cortex³⁸ and in various glia elements³⁹ in human and experimental conditions (in fresh, unfixed tissue, glycerophosphate and adenylic acid media, pH 4.7-6.0).

Wall et al.⁴⁴ noticed that when the lumbar region of the frog spinal cord was subjected to large doses of ultrasound, immediately after exposure the hind legs were completely anesthetic and paralyzed. Histologic examination of the cord two to seven days after treatment showed complete destruction of all nerve cells, of many glia cells, loss of supporting elements, so that the cord lost its normal texture and became very soft. Subjecting the same region of the cord to smaller doses of ultrasound, the exposure was followed by immediate paralysis, but sensation in the hind limb remained. Histologic studies of the cord showed that the large cells of the anterior horn had been severely damaged, leaving the small cells in the cord intact. Still

smaller doses produced no obvious signs of paralysis or sensory changes, although histologic studies showed that a large percentage of the anterior horn cells within a limited extent of the cord had been damaged.

REFERENCES

- ¹ Appel, L. and Van Bogaert, L.: Etudes sur paraplegie spasmodique familiale. II. La famille Ameil: formes très précoces et congénitales. Contribution histopathologique. *Acta Neurol. et Psychiat. Belge.* 51:129-166, 1951.
- ² Brain, R., Daniel, P. M., and Greenfield, J. G.: Subacute cortical cerebellar degeneration and its relation to carcinoma. *J. Neurol., Neurosurg. & Psychiat.* 14:59-75, 1951.
- ³ Bunting, H.: Histochemical analysis of pathological mineral deposits at various sites, with discussion of methods used. *Arch. Path.* 52:458-469, 1951.
- ⁴ Cardona, F.: Problema istologico delle encefalomieliti. *Riv. di. pat. nerv. LXXII*:265-288, 1951.
- ⁵ Cazzullo, C. L. and Allegranza, A.: Forme croniche di encefalomielite spermentale 'allergica' nella cavia. *Biol. latina.* 4:76-108, 1951.
- ⁶ Cowen, D. and Wolf, A.: Experimental congenital toxoplasmosis IV. Genital and secondary lesions in the mouse infected with toxoplasma by the vaginal route. *J. Neuropath. & Exper. Neurol.* 10:1-15, 1951. Experimental congenital toxoplasmosis V. Lesions in the offspring of mice infected with toxoplasma by the vaginal route. Observations on an associated hepatic injury. *J. Neuropath. & Exper. Neurol.* 10:142-157, 1951.
- ⁷ Danis, P. and Van Bogaert, L.: Angiome choroidien "muet" au cours d'une maladie de Sturge-Weber, suivie pendant toute la vie du sujet. (Étude anatomoclinique). *Acta Neurol. et Psychiat. Belge.* 51:74-94, 1951.
- ⁸ Reale, G. and D'Argenio, L.: Sull'azione del malononitrile nell'encefalo di coniglio (studio sperimentale ed istopatologico). *Riv. di. pat. nerv. LXXII*:331-341, 1951.
- ⁹ Denny-Brown, D.: Hereditary sensory radicular neuropathy. *J. Neurol. Neurosurg. & Psychiat.* 14:303-307, 1951.
- ¹⁰ Eros, G.: Observations on cerebral arteriosclerosis. *J. Neuropath. & Exper. Neurol.* 10:257-294, 1951.
- ¹¹ Ferraro, A. and Roizin, L.: Histopathologic aspects of experimental allergic encephalomyelitis during and following cortone acetate treatment (preliminary report). *Ann. Meet. Amer. A. Neuropath., Atlantic City, June 17, 1951.*
- ¹² —: Production of experimental encephalomyelitis with calcium acetate compound extracted from brain tissue. *J. Neuropath. & Exper. Neurol.* 10:394-407, 1951.
- ¹³ Flores, V., Reda, G. C., and Mengoli, G.: Le leucoencefaliti sclerosanti subacute. Contributo anatomo-clinico. *Riv. neurol.* 20:465-500, 1951.
- ¹⁴ Foley, J.: Cerebral calcification in a family. *J. Neurol., Neurosurg. & Psychiat.* 14:253-261, 1951.
- ¹⁵ Freeman, W. and Williams, J. M.: Lesions of transorbital lobotomy. *Arch. Neurol. & Psychiat.* 66:191-198, 1951.
- ¹⁶ Furtado, D. and Marques, V.: La tuberculose du système nerveux au Portugal. *Semaine d. hôp. Paris.* 27:26-28, 1951.
- ¹⁷ Gereb, T.: Die Beziehungen der nekrotisierenden Myelopathie zur multiplen Sklerose. *Monatschr. f. Psychiat. u. Neurol.* 120:237-248, 1950.
- ¹⁸ Globus, J. H., Gang, K. M., and Bergman, P. S.: Torula Meningoencephalitis. *J. Neuropath. & Exper. Neurol.* 10:208-228, 1951.

- ¹⁹ Greenfield, J. G.: The classification of diffuse demyelinating sclerosis of the brain on the basis of pathogenesis. *Folia psychiat.* 53:255-267, 1950.
- ²⁰ Haddenbrock, S.: Zur Pathogenese systematischer Bahndegenerationen bei amaurotischer Idiotie und zur Frage der Beziehungen dieses Leidens zur Myoklonusepilepsie. *Arch. f. Psychiat.* 185:129-164, 1950.
- ²¹ Hawke, W. A. and Donohue, W. L.: Bilateral necrosis of the corpora striata. Report of a fatal case and reference to a possible syndrome of the corpora striata. *J. Nerv. & Ment. Dis.* 113:20-39, 1951.
- ²² Hicks, S. P. and Warren, S.: Infarction of the brain without thrombosis: an analysis of one-hundred cases with autopsy. *Arch. Path.* 52:403-412, 1951.
- ²³ Horstman, D.: Neuropathology of Teschen disease (Virus encephalomyelitis of swine). *Proc. Soc. Exper. Biol. & Med.* 77:8-13, 1951.
- ²⁴ Hyde, J. B. and Campbell, B.: Virus as a primary plasmacytogenic agent in brain tissue. *J. Neuropath. & Exper. Neurol.* 10:408-415, 1951.
- ²⁵ Jager, W. A. Den Hartog: Clinical and pathological findings in a case of dystrophia myotonica. *Arch. Neurol. & Psychiat.* 66:178-190, 1951.
- ²⁶ Kabat, E. A., Wolf, A., and Bezer, A. E.: Effect of cortisone on experimental acute disseminated encephalomyelitis. *Ann. Meet. Amer. Neurol. A., Atlantic City*, June 19, 1951.
- ²⁷ Latimer, F. R., Webster, J. E., and Gurdjian, E. S.: Neurological complications of rabies vaccine: report of two cases. *Arch. Neurol. & Psychiat.* 65:16-28, 1951.
- ²⁸ Ley, A. Jacas, R., and Oliveras, C.: Torula granuloma of the cervical spinal cord. *J. Neurosurg.* 8:327-335, 1951.
- ²⁹ Liban, E., Halpern, L., and Rozanski, J.: Vascular changes in the brain in a fatality following electroshock. *J. Neuropath. & Exper. Neurol.* 10:309-318, 1951.
- ³⁰ Luzzatto, A.: La streptomycina nella tubercolosi del nervasse e delle meningi. *Riv. di pat. nerv. LXXII*:1-155, 1951.
- ³¹ Margolis, G., Odom, G., Woodhall, B., and Bloor, B. M.: The role of small angioma-tous malformation in the production of intracerebral hematomas. *J. Neurosurg.* 8:564-575, 1951.
- ³² Messimy, R., Berdet, H., Feld, H.M., Heuyer, G., and Petit-Dutaillis, D.: Étude anatomo-pathologique de fragments cérébraux prélevés par topectomies pré-frontales chez les schizophrènes. *Rev. neurol.* 84:230-243, 1951.
- ³³ Moyer, W. A., Jervis, G. A., Black, J., Koprowski, H., and Cox, H. R.: Action of adrenocorticotrophic hormone (ACTH) in experimental allergic encephalomyelitis of the guinea-pig. *Proc. Soc. Exper. Biol. & Med.* 75:387-390, 1950.
- ³⁴ Myle, G. and Lowenthal, A.: Lipomatose et lipolyphangiomatose faciale a localisation trigeminale associées a des fragments de phacomatoses voisines (deux cas). *Acta Neurol. et Psychiat. Belge.* 51:473-485, 1951.
- ³⁵ Naidoo, D. and Pratt, O. E.: The localization of some acid phosphatases in the brain tissue. *J. Neurol., Neurosurg. & Psychiat.* 14:287-294, 1951.
- ³⁶ Netsky, M. G., Shapiro, D., and Zimmerman, H. M.: Hallervorden-Spatz Disease & Dystonia. *J. Neuropath. & Exper. Neurol.* 10:125-141, 1951.
- ³⁷ Papez, J. and Bateman, J. F.: Changes in nervous tissues and study of living organisms in mental disease. *J. Nerv. & Ment. Dis.* 114:400-412, 1951.
- ³⁸ Roizin, L.: Comparative morphologic and histometabolic studies in biopsy and topectomy material. *J. Neuropath. & Exper. Neurol.* 10:177-189, 1951.
- ³⁹ —: Essays on comparative morphologic and histometabolic aspects of neuroglia of the central nervous system. *Ann. Meet. Amer. A. Neuropath., Atlantic City*, June 17, 1951.

- ⁴⁰ Schenk, V. M. D.: *Maladie de Pick. (Étude anatomo-clinique de 8 cas)*. Ann. méd.-psychol. 1:574-587, 1951.
- ⁴¹ Schmidt, I. G. and Schmidt, L. H.: Neurotoxicity of the 8-aminoquinolines III. The effects of pentaquine, isopentaquine, primaquine, and pamaquine on the central nervous system of the Rhesus monkey. J. Neuropath. & Exper. Neurol. 10:231-256, 1951.
- ⁴² Simma, von K.: Ueber Thalamusveränderungen bei saniler Demenz und bei der Alzheimerschen Krankheit. Monatschr. f. Psychiat. u. Neurol. 122:156-178, 1951.
- ⁴³ Tolone, S. and Ventura, D.: XVI. Morphologia delle reazioni fosfatasiche nel tessuto nervoso (Ricerche istochemiche). Acta neurol. 6:529-617, 1951.
- ⁴⁴ Wall, P. D., Fry, W. J., Stephens, R., Tucker, D., and Lettvin, J. Y.: Changes produced in the central nervous system by ultrasound. Science. 114:686-687, 1951.
- ⁴⁵ Wildi, E.: Nids astrocytaires pericapillaires de l'écorce cérébrale des arterioscléreux cérébraux. Confinia neurol. 2:139-150, 1951.
- ⁴⁶ Wohlfart, G.: Dystrophia myotonica and Mytonia congenita: histopathologic studies with special reference to changes in the muscles. J. Neuropath. & Exper. Neurol. 10:109-124, 1951.
- ⁴⁷ Vortel, V.: Über Gehirnveränderungen bei der Eklampsie, Schweizer Arch. Neurol. & Psychiat. 67:174-187, 1951.
- ⁴⁸ Vogel, S.: Cerebral demyelination and focal visceral lesions in a case of acute hemorrhagic pancreatitis, with a consideration of the possible role of circulating enzymes in the causation of the lesions. Arch. Path. 52:355-362, 1951.
- ⁴⁹ Wolf, A., Kabat, E. A., and Fonseca, J. R. C.: The effect of cortisone in activating trypanosomal encephalitis and myocarditis in Rhesus monkeys. Ann. Meet. Amer. A. Neuropath., Atlantic City, June 17, 1951.
- ⁵⁰ Zarabashvili, A. D.: Pathoarchitectonics of schizophrenia. Nevropat. i. psikhiat. 19:26-31, 1950.

Pharmacology of the Nervous System

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ADVANCES in clinical understanding and therapy are inevitably linked and, in fact, dependent upon fuller understanding of function in the nervous system and the influence exerted by drugs. We have not failed, therefore, to examine every laboratory experiment from the point of view of clinical potentialities and every therapeutic trial for inferences as to fundamental processes in normal and diseased functions. Progress this year has been most marked in the clarification that comes from agreement on the questions proposed and from the growing recognition that junctions—neuroeffector and synaptic—are so similar that differences, as characterized by drug response, are chiefly of threshold rather than of kind. Thus, although perhaps not acknowledged as such by all participants, one is left with just this impression from the conference on *Curare and Anticurare Agents*.¹

An exceedingly worthwhile conference was held on the *Nerve Impulse*.² The participants wasted no time in getting down to fundamentals and continuing on a completely informal question and answer basis which succeeded in bypassing most, if not all, the non-productive pronouncements and debates in favor of creative analysis. The swing of the argument back and forth is a most convincing sign that the nature of transmission phenomenon, far from being settled, is still a very live and controversial question. Another illuminating conference on the morphologic, pharmacologic and electrophysiologic aspects of *Transmissions Synaptiques, Ganglionnaire et Centrale*³ was held in Brussels. The very effective interdisciplinary approach of the Milbank Memorial Fund Symposium on the *Biological Aspects of Mental Health and Disease*⁴ has now been published.

The crop of review articles includes two by Feldberg: *Present Problems Concerning the Chemical Transmission of Nervous Impulses*⁵ and *The Physiology of Neuromuscular Transmission and Neuromuscular Block*.⁶ The latter is the shorter of the two but succeeds in giving a clear story presented from a point of view consistent with chemical transmission by acetylcholine (ACh). Pharmacological Reviews deals with: *Some Basic Aspects of the*

Pharmacology of Synthetic Curariform Drugs by Taylor⁷ and *The Nature of Adrenergic Nerve Mediators* by von Euler.⁸ Both of these make a conscientious effort to relate the sometimes intricate findings to clinical problems. Whittaker has dealt carefully, skillfully and profitably in a Physiological Review article: *Specificity, Mode of Action and Distribution of Cholinesterase*.⁹ He concludes very instructively that generalizations as to the specificity of cholinesterases (ChEs) are "too narrowly conceived," and he goes on to say "we have now entered a period in which previous ideas about the role of cholinesterase and even of acetylcholine are once more in a state of flux." *New Anesthetic Drugs* are briefly reviewed by Griffith.¹⁰

New departures in thinking or experimentation hold out further promise. In his study of the role of electric fields in transmission phenomena, Eccles¹² has taken the logical, but technically extremely difficult, step of recording the electrical changes from the interior of nerve cells by inserting a micro-electrode into the soma of motoneurons in the cord. Characteristically, he has set himself a crucial question and abided by the answer, provisionally. Thus, his strong advocacy of electrical transmission at the synapse rested on appropriate field effects to account for excitation and inhibition, respectively. Such effects would be expected to extend across the membrane and into the soma without change of sign. Intracellular recording in his laboratory does not confirm this so that, particularly for inhibition, a special process must be initiated at the cell membrane in response to a specific activator rather than to current flow. He is, therefore, led to believe that the facts of inhibition can be fitted only by a humoral mechanism. Marrazzi had demonstrated the synaptic inhibitory action of adrenaline and proposed it as a humoral inhibitor for the nervous system as far back as 1939 (sympathetic ganglia¹³) and 1943 (optic cortex¹⁴). Further work has led him to the view that a reciprocal relation is to be looked for at synapses between cholinergic excitation and adrenergic inhibition.⁴ The technic of evoking an optic cortical potential in an essentially monosynaptic preparation has enabled Marrazzi and Hart to document further this reciprocal relationship as well as the similarity between cortical and ganglionic synapses by demonstrating an ACh-like stimulating action of pilocarpine at a group of cholinergic cerebral synapses¹⁵ and inhibitory actions of amphetamine and ephedrine at the same site.¹⁶ The generally recognized stimulating actions of the last two must either occur at different parts of the brain or be the result of a release phenomenon following interruption of pathways by synaptic inhibition. A remarkable development is the recording on cortical stimulation of an adjacent cortical response which Chang¹⁷ is satisfied he can analyze into a dendritic component and a second component originating in the deeper lying soma. His suggestion that the axon-soma junction is susceptible to

block attributes to it the vulnerability ordinarily associated with the synapse. It is hoped that the interpretation will be put to the further test of recording from within the soma.

In lieu of satisfactory objective criteria for the defining of the depth of narcosis, Verzeano¹⁸ has resorted to Bickford's servo-motor integration of the electroencephalogram for stabilization of the depth of narcosis while another integrator simultaneously measures electrical output of the brain in a more accurate fashion. Burns¹⁹ has made an extremely interesting preparation by neurologically isolating a portion of the cortex *in vivo* through undercutting that does not interrupt the blood supply. His studies of the electrical responses and their modification by anesthetics seem particularly rewarding. McIlwain²⁰ has extended studies of respiration in brain slices by demonstrating an increase in response to electrical stimulation of the slice *in vitro*. Koelle²¹ has been alert to possible improvements in his technic of histochemical localization of ChE's and by minor changes has eliminated artifacts due to diffusion of the enzymes. This is recognized as a serious drawback to any histochemical technic.

TRANSMISSION PHENOMENA AT THE SYNAPSE

Neurohumors and Facilitating and Blocking Agents

Cholinergic. Studies of cholinergic phenomena in the brain utilizing ACh as such are few, possibly because its existence in the body is ordinarily ephemeral. Sherwood, Ridley and McCulloch²² have extended by similar experiments on "catatonic" cats studies by Rowntree et al.²³ of the aggravating effects of antiChE's on schizophrenics and Sherwood's²⁴ studies of the ameliorating effect in this condition of injection of ChE, etc. into the cerebral ventricles. Cats rendered catatonic by suitable electrolytic lesions showed an exaggeration of symptoms on the intraventricular injection of 0.5-2 mg. of ACh while ChE induced transient remission with sustained improvement on repeated injections. Control cats, on the other hand, showed on intraventricular administration of ACh, agitation and behavior interpreted as "hallucinatory" along with signs of autonomic activation. Similar, but more marked and prolonged, actions were obtained by 3.75-7.5 mg. of methacholine and 0.05-0.1 mg. of carbachol. In a reevaluation of the causative factors in idiopathic epilepsy, Forster²⁵ no longer advocates ACh. Further evidence that ACh is a transmitter to the supraoptic neurons is offered by Pickford and Watt,²⁶ who demonstrate that the action of ACh in inhibiting the rate of urine flow in an unanesthetized dog is greater when injected into the carotid artery than when given intravenously, and that even smaller doses are effective in the presence of eserine.

The use of antiChE's in the study of cholinergic function is not only

more convenient but, so long as antiChE's are not shown to have any other major component to their action than the inhibition of ChE's, even more compelling in its significance. In this situation, we are dealing with the preservation and accumulation of naturally occurring ACh. Chennells, Floyd and Wright²⁷ have elicited clearcut enhancing and, in larger doses, depression of reflexes on the intrathecal injection of diisopropylfluorophosphate (DFP) in cats. The flexor reflex elicited by a train of afferent stimuli is better maintained while the electromyogram indicates that the enhancement evident in mechanical records could be "due to recruitment of further anterior horn cells." Various manifestations were not synchronous so that enhancement and depression of different reflexes could co-exist. Convulsions were sometimes seen though they were not as violent as those following intravenous injection.

In further testing, the similarity of effects at various junctions thought to be cholinergic, peripheral and central, Marrazzi and Hart¹⁵ have shown that just as pilocarpine mimics ACh at neuroeffector junctions it has a stimulating action similar to that of ACh when tested on the intercortical two neuron transcallosal preparation. Here the differential action, i.e., an effect confined to the postsynaptic component of the potential shows the pilocarpine action to be synaptic. The very characteristic blocking action of atropine on cholinergic transmission offers another very valuable lead as to the nature of transmission phenomena. This year's literature offers several such examples. Thus, Funderburk and Case²⁸ have been able to show in cats and monkeys that atropine, though not eucatropine or dibutoline (dibutylurethane) when intravenously administered is able to decrease or abolish spiking of the EEG from topical application of ACh, but not the apparently nonspecific spiking due to application of curare or penicillin. They believe that comparable to this is the atropine action they observed inducing in the EEG a sleep-like pattern which was prevented by eserine. They failed to get any actions with neostigmine and attribute a lack of effect with this and with dibutoline to a possible failure to penetrate the blood-brain barrier. The failure of eucatropine action they attribute to inadequate dosage. Robinson and Hughes²⁹ essentially confirmed the atropine eserine results but only in larger doses than those used by Funderburk and Case. Sawyer et al.³⁰ have repeated their experiments on what they consider to be a central blocking action of atropine on the copulation-ovulation reflex in the rabbit with beta-diethylaminoethyl xanthene-9-carboxylate methobromide (Banthine), in experiments where thiopental (pentothal), procaine and pyranisamine (neoantergan) proved ineffective.

The central neurorespiratory mechanism has given some clearcut data in the hands of Krivoy, Hart and Marrazzi.³¹ They recorded phrenic and intercostal nerve action potentials and were thereby able to show a central

component to the paralytic action of DFP. Further experiments with the phrenic nerve preparation demonstrated that this paralysis could be relieved by atropine and, if the dose of DFP was carefully controlled and the animal maintained on artificial respiration, spontaneous recovery could also be demonstrated. The cholinergic characteristics of the central respiratory mechanism were further confirmed by demonstration in the phrenic nerve preparation that in the respiratory paralysis produced by d-tubocurarine (crystalline) there is an early central component from which recovery occurs early leaving a paralysis on a peripheral or neuromuscular basis. The early occurrence and rapid recovery probably account for Paton and Zaimis⁶⁰ failure to record this cessation of respiratory discharge in the phrenic nerve. Heymans et al. without benefit of a discriminating technic, such as offered by action potentials, are unable to demonstrate an action of atropine or trihexylphenidyl (artane)⁸² or of nicotine³³ on the cardio-inhibitory center of dogs. However, they,³⁴ in another connection, point out "the ways in which secondary pharmacological actions" (such as may be expected in their experiments) "may complicate interpretation of the results."

In the spinal cord, on the other hand, Bonnet³⁵ uses an elevation of synaptic potentials to illustrate what is interpreted as a direct non-specific stimulant action of atropine. However, such a result could readily come about from the known preferential cumulative effect on multi-synaptic pathways, which might then release the segmental level to allow an increased synaptic response to a given stimulus. Bernhard and Taverner³⁶ observe an increase in the amplitude of the monosynaptic spinal response on the intravenous administration of d-tubocurarine in unanesthetized cats, an effect abolished by Dial. This would agree with the contention of McIntyre et al³⁷ that d-tubocurarine stimulates before it depresses. Clinical use of the recognized preferential action of mephenesin on multisynaptic pathways is described by Davison³⁸ and by Boles and Smith³⁹ in the treatment of tetanus. Funderburk, King and Unna⁴⁰ describe a similar preferential action on multisynaptic pathways for the benzazoles (6-methyl-2-aminobenzothiazole) with data suggesting also depression of the brain stem activating center.

The significance of the ACh content of excised brain has been materially clarified by Elliott and Henderson⁴¹ who state: "It seems probable that the free ACh found is largely an artifact, and most of it is liberated in the process of extraction, more or less in proportion to the amounts of bound ACh present but in amounts which vary with physical factors in the homogenization. It was found that a further amount of free ACh could be obtained on rehomogenization of the extracted residue." They suggest further that *in vivo* a "reversible equilibrium exists between free and bound ACh" and

that on protection by eserine the small amount of accumulated free ACh slows down the liberation of further free ACh and so allows the bound ACh to be built up. They go on to say: "There is no direct evidence that insoluble bound ACh is necessarily the primary product. It could be the product of a reversible complex formed between free ACh and insoluble material not involved in synthesis but perhaps present close to the site of synthesis." Thus, they believe that virtually all the ACh in the brain is in bound form and that the release from the bound form is reversible. They speculate on the possibility that in intact tissue synthesis of ACh and binding might occur at the cell surface where the influence of potassium and calcium in the extracellular fluid could readily be understood as an effect on the spatial relationship of the components of a surface located ACh system. A very interesting development in this field is McIlwain's²⁰ use of electrically "stimulated" brain slices and the finding that respiration can be increased by such stimulation and that the metabolic characteristics of such increased respirations are the same in response to stimulation *in vitro* as in the brain *in situ*.⁴² Greig and Mayberry⁴³ cite in favor of their thesis that antiChE's increase permeability, that intravenous administration of physostigmine reduces by 50 per cent the anesthetic lag on intravenous injection of barbitol in mice and that this is accompanied by an increased penetration of the barbitol into the brain. Similar inferences by Greig and co-workers as to the increase in corneal permeability produced by antiChE's is denied by Keasling et al.⁴⁴ who find that physostigmine locally or subcutaneously does not endow procaine with corneal anesthetic properties although the subcutaneous administration of physostigmine or pilocarpine produces some corneal anesthesia in the rabbit, as measured by loss of corneal reflex. Permeability changes are also invoked by Aird and Strait⁴⁵ who find that sodium diphenyl hydantoinate (dilantin) reduces by 20 per cent the amount of spectrophotometrically determined cocaine entering the cerebral cortex, the blood concentration remaining unaltered. They feel that this apparent reduction in the permeability of the blood-brain barrier may be the means by which dilantin exerts its anticonvulsive action but they recognize that a direct cortical depressant effect is not ruled out. Similarly, Aird and Gordan^{46, 47} appear to favor a possible effect of desoxycorticosterone on cerebral permeability and on the blood-brain barrier to account for beneficial results in epilepsy.

Root⁴⁸ describes cats in which, through an apparently preponderant action of tetraethylammonium (TEA) on the parasympathetic system, a pressor action of pilocarpine is uncovered even in adrenalectomized animals. He interprets the pilocarpine action as stimulation of sympathetic ganglia and quotes in support the 1939 work of Marrazzi⁴⁹ and the 1949 work of Ambache.⁵⁰ As in Marrazzi's experiments, atropine blocks the ganglionic

stimulation. A current confirmation of Marrazzi's description of the block of sympathetic ganglia by atropine is offered by Gyermek and Sztanyik.⁵³ Feldberg⁵⁴ enters into a complicated debate with Ambache et al.^{55, 56} on the actions of nicotine, pilocarpine, barium and atropine on ganglia in the small intestine (cf. 160). Two new autonomic ganglionic stimulants have been described. Alpha-trimethylammoniumpropanediol,⁵¹ which is capable of exhibiting typical ACh-like depressor and other actions produces a reversal, i.e., pressor effect in atropinized animals. The stimulant action of dimethylphenylpiperazinium (DMPP)⁵² can be prevented by the previous administration of TEA or hexamethylene-bis-trimethylammonium bromide (hexamethonium). Dimethylpiperidylidene diphenylmethane methylsulfate (prantal) is said⁵⁷ to selectively block parasympathetic ganglia associated with gastric secretion and motility at doses which do not produce mydriasis. On intravenous administration the more extensive effects include block of sympathetic ganglia as well. Specificity is thus relative and there is, so far, no real exception to the idea that qualitatively similar actions will be found at all cholinergic sites, including both sympathetic and parasympathetic ganglia, when carefully looked for. This is not to deny Paton and Zaimis' statement⁵⁸ that "despite the profound analogies between transmission processes at the myoneural and at the ganglionic synapses, there are evidently significant and fundamental differences between them." This was said in comment upon their findings that the longer chained members of the polymethylene-bis-trimethylammonium series are most effective in inducing neuromuscular block while the shorter chained are most effective in inducing ganglionic block.

Nevertheless, the family resemblance of the short and long chain members is more than chemical for, as quoted by Paton,⁶² pentamethonium like decamethonium can antagonize the neuromuscular blocking action of d-tubocurarine. The ganglionic block by penta- and hexamethonium is not, as in the case of the decamethonium block at the neuromuscular junction, accompanied by a preliminary stimulating (depolarizing) action. The ganglionic blocking action of pentamethonium is nicely illustrated in humans by Grob and Harvey.⁵⁹ Riker and Wescoe⁶¹ report a paucity of effects of tris (triethylamino ethoxy) benzene (Flaxedil) on the autonomic nervous system. The data in their reports need not be taken to indicate total absence of effects on autonomic ganglia but rather as evidence of low potency in this respect. Even with vagal block the possibility of a contributory effect upon the vagal ganglion does not appear to be totally excluded. In fact, the accumulated papers in the curare symposium¹ lead one to conclude that, though there are marked differences in the potencies of various compounds with respect to ganglionic block, all compounds do have this action

to some degree. The extent of this action is in some cases of theroetic rather than of clinical importance.

The use of drugs to help identify the nature of an anatomic connection in the autonomic nervous system dates back to Langley. An interesting modern example is offered by De Castro's⁸¹ successful attempts to effect functional connection between afferent vagus fibers and postganglionic cells of the superior cervical sympathetic ganglion in the cat. Electrical stimulation of these afferent fibers produced postganglionic ocular changes which were, however, not influenced by the exhibition of the antiChE. In agreement with Feldberg's discussion, one would wonder whether the connection was one dependent on synaptic transmission or simply the delivery of an electrical stimulating shock to the postganglionic cells through the afferent fibers acting merely as conductors of applied current.

Antihistaminics with atropine-like effects are receiving continuous trial in the treatment of parkinsonism. Three reports⁶³⁻⁶⁵ describe the usefulness of diphenhydramine (Benadryl) with the suggestion that the best results are obtained when this drug is combined with Artane or one of the belladonna products. Bovet and Longo⁶⁶ insist, however, that the mechanism of action of dipareol and parpanit in parkinsonism is totally different from that of atropine and scopolamine. Despite this, they favor identity of actions at ganglia and in the central nervous system and interpret their results to indicate that antagonism to the central actions of nicotine is the preferred animal screening procedure for determining drugs effective in parkinsonism. McCawley et al.⁶⁷ have tested the anti-emetic effects of diphenhydramine by electrical stimulation of the vomiting center localized by Borison and Wang⁶⁸ and also following subcutaneous apomorphine. They suggest a "central atropine-like property" to account for the effectiveness and find that "the morpholine analogue of diphenhydramine having only weak atropine qualities did not elevate the vomiting threshold nor was it useful in controlling clinical emesis."

Borison and Wang⁶⁹ have also located a site, quite distinct from their previously described vomiting center, in the dorsal region of the ala cinerea of dogs, which functions as a "chemoreceptor trigger zone." This site appears to be the locus of action of the emetics usually described as "centrally acting", such as apomorphine, lanatoside C, scillaren A and ouabain. Emesis from oral copper sulfate solution was not interfered with by absence of the trigger zone; nor was that of "Veriloid".⁷⁰ A comparable and similarly located area was also found in cats.⁷¹

Although one thinks of it in connection with the actions of Benadryl, the point of action of dimenhydrinate (Dramamine) on motion sickness remains undefined. The work of Gutner et al.⁷² points to an action on the

labyrinth as contributing to the effect. The scope of usefulness of this drug, however, is expanding. Gay⁷³ has reported beneficial effects in various types of dizziness of labyrinthine or central origin. Kerman⁷⁴ has reported successful prophylaxis of post-electro-shock nausea and vomiting. Rudolph et al.⁷⁵ report "excellent" results in prophylaxis and treatment of postanesthesia nausea and vomiting with 100 mg. doses. Wollgast and Prockter⁷⁶ found 50 mg. not effective.

Adrenergic. Lennox et al.⁷⁷ report that in 11 out of 19 monkeys amphetamine given subcutaneously eliminated the extreme postconvulsive EEG slowing observed after electroshock and the animals appeared more alert. The authors are not able to distinguish between possible central nervous system stimulation and vasomotor effects of amphetamine. Marrazzi and Hart,¹⁶ on the other hand, have demonstrated in cats inhibition of synapses in the optic cortex by amphetamine and ephedrine unrelated to circulatory phenomena as indicated by blood pressure changes. It does not necessarily follow, of course, that the action of these substances is the same throughout the brain although apparent stimulation could be on the basis of a release phenomenon through inhibition of synapses in appropriate pathways. Lundberg⁷⁸ confirms the 1939 work of Marrazzi¹³ and the 1942 work of Bulbring and Burn⁷⁹ in obtaining inhibition of transmission in the superior cervical sympathetic ganglion by adrenaline. Like Marrazzi, he also obtains a similar, though weaker, inhibition with noradrenaline. On close arterial injection as little as 0.1 gamma of adrenaline was effective and 1 to 2 gamma could produce complete block. The ganglionic effect of adrenaline could be abolished by dihydroergotamine. Tum Suden and Marrazzi¹⁴⁵ have successfully prepared a parasympathetic ganglion, the ciliary in the dog, so that synaptic transmission could be followed by recording the postsynaptic action potential in the ciliary nerve on electrically stimulating the presynaptic oculomotor nerve. On introducing adrenaline into its intact circulation the synapses in this ganglion also showed a primary inhibition not preceded by any preliminary enhancement. With Hart and Lindenberg,⁸⁰ they further showed that ephedrine also produced inhibition here as in sympathetic ganglia. These data suggested the presence of adrenergic inhibitory pre-ganglionic fibers in the ciliary ganglion and their preliminary data with chromaffin staining tends to confirm this. The results in the ciliary ganglion illustrate that adrenergic inhibition occurs in the ganglia of both divisions of the autonomic nervous system and that the reciprocal relation between cholinergic excitation and adrenergic inhibition holds at both of these sites as well as at synapses in the cortex (optic and auditory) and at autonomic neuroeffector junctions. Swan,^{82, 82a} in an analysis of the after dilatation on cessation of an adrenaline infusion concludes, from the fact that it does not occur in the sympathectomized limb, that the dilator effect originates in a

central action of the adrenaline. This might well be a reduction in vasoconstrictor impulses from block of sympathetic ganglia, largely obscured during the infusion by the constrictor action on the blood vessels themselves. Taylor and Page⁸³ have produced a vasodilator action in the dog's body when adrenaline or noradrenaline was introduced into the perfusion limited to the dog's brain. This central action obviously takes place in the brain. They speak of cerebral chemoreceptors which buffer the actions of adrenaline and noradrenaline by causing vasodilatation and of histamine and acetyl-beta-methylcholine by causing vasoconstriction. As far as the choline and adrenals are concerned, this might well represent cholinergic excitation and adrenergic inhibition of synapses in the "vasoconstrictor center." Heymans et al.⁸⁴ have induced a reflex fall of arterial pressure by application of adrenaline and noradrenaline to the carotid sinus, an effect prevented by the previous application of adrenolytic compounds. Gradually, more and more bits of evidence collect to indicate that cholinergic excitation and adrenergic inhibition may operate at the carotid sinus.

STIMULANTS

Further developments in technic have brought new information on the classical stimulant, strychnine. Bremer⁸⁵ has recorded and analyzed on the volume conductor principle evoked responses in the auditory cortex distinguishing a potential wave attributable to neurons impinging on cortical pyramidal cells and a second wave due to the efferent impulses in the pyramidal cells. In this way, he has shown the greater sensitivity of the latter to the facilitating actions of strychnine. By the analysis of his evoked local cortical potentials, where an influence on the second or soma component could be recorded without significant change of the dendritic portion of the cortical potential, Chang⁸⁶ also ascribes strychnine action to an effect on the soma of pyramidal cells, i.e., an acceleration of the "process of impulse initiation" thus increasing synchronization and the efficiency of summation. Wall and Horwitz⁸⁷ report that in sympathetic ganglia where a 1:1 type of transmission may occur transynaptic transmission of strychnine spikes may take place. They also found some evidence that strychnine might, as found previously by Bremer, influence excitability at a distance "by a probably electrotonic effect." Frankenhaueser⁸⁸ cautions that strychnine neuronography has limitations in that apparently direct pathways may exist which cannot be traced by the action of strychnine, in this case the tracts from the olfactory bulb and the pathways to the distal part of the vagus nerve. Thus, negative evidence with this technic is not conclusive. Dow⁸⁹ has previously claimed that strychninization of the cerebellum did not elicit strychnine spikes. Swank and Brendler⁹⁰ have recorded picrotoxin and metrazol spikes from the cerebellar cortex, often before they were

detectable in the cerebral cortex. On this basis, they suggest that these discharges may originate in the brain stem and spread from there to both the cerebellum and cerebrum. Hoff et al.⁹¹ have performed experiments to show that strychnine facilitation of pressor responses evoked from the cerebral cortex is due to a local action on the cortex. The intravenous injection of dehydroascorbic acid (DHA) in rats produces evidences of central nervous system stimulation which are attributable to the liberation of ascorbic acid on the reduction of neutral DHA.⁹² Propylene glycols produce a spreading type of increased electrocortical activity of dogs not amenable to the central depressant action of atropine.⁹³ In their study of glycolysis and respiration in the brain, Webb and Elliott⁹⁴ could find no marked effects of convulsant drugs except at high concentrations, but McLennan and Elliott⁹⁵ demonstrate striking effects on ACh synthesis by intact slices of rat brain cortex and by cell-free preparations from beef brain. The accelerated synthesis occurs over a narrow low range of drug concentrations, while higher concentrations inhibit. This latter effect is apparently additive so that stimulating concentrations of two drugs, when exhibited together, induce inhibition. The convulsants studied included picrotoxin, pentylene tetrazol, thujone, camphor and methionine sulfoximine. An extremely interesting, though so far unexplained, finding is that of Chance⁹⁶ that the brains of mice subjected to convulsants show characteristic patterns of increased glycogen, approximately following the supposed distribution of sites of action of the convulsants.

DEPRESSANTS

Important contributions have been made to the recurrent question of the relation between brain metabolism and narcosis. McLennan and Elliott⁹⁵ obtained quite small effects on oxygen uptake and glycolysis at concentrations which might be present in the tissue fluids of narcotized animals but which do inhibit ACh synthesis considerably. They regard the latter effect as more significant. At smaller narcotic concentrations there is a slight, unexplained increase in synthesis. Brink⁹⁷ has "adopted the attitude that some insight" can be gained into the complex problem of general anesthesia by studying first the easier problem of local anesthesia. This is useful and particularly so to the extent that it defines the differences between local anesthesia at the axon and "local anesthesia" at the synapse. The generally lower threshold of the synapse to general anesthetics constitutes a distinguishing feature of the latter. This is illustrated in Larrabee and Posternak's⁹⁸ studies of the effects of narcotics on transmission through the sympathetic ganglion recorded as a postsynaptic action potential in response to supramaximal presynaptic stimuli. Chloretone, chloroform, ether, pentobarbital, amyl and hexyl alcohol and cocaine "depress synaptic transmis-

sion more readily than conduction along any type of axon" the latter represented in some cases by the potential of the fibers running through the ganglion and past the recording electrode before synapsing. On the other hand, urethane and methyl, ethyl, propyl or butyl alcohols did not show a selective action on synaptic transmission. Methyl and ethyl alcohols in a very limited number of experiments actually showed a synaptic facilitation so that the depressant action in this case appears to be selective on conduction. Synaptic facilitation was demonstrated in experiments using submaximal stimuli while all the others were performed with supramaximal stimuli to the preganglionic fibers. This, in some cases, could have obscured minimal degrees of depression. Some very interesting and instructive systematizations of data are attempted. Van Harreveld et al.⁹⁹ present data intended to distinguish a "membrane stabilizing" action of pentobarbital and a depolarizing action of ether and of diphenylhydantoin. The latter two have an additive action in suppressing knee jerks while diphenylhydantoin given after a pentobarbital depressed reflex often actually increased it. However, the only evidence for a depolarizing action of ether is the work on peripheral nerves while Van Harreveld interprets as depolarization his own previous work showing that ether reduces asphyxial depolarization of the spinal cord. Beecher's group (Bunker et al.)¹⁰⁰ failed to find acidosis from ether anesthesia in man although they did find it in dogs. In contrast, cyclopropane produced the respiratory acidosis in both species. Another species difference is noted by Morris, Frederickson and Orth,¹⁰¹ for blood concentrations required for equivalent depths of anesthesia, the level for chloroform in patients being one-third to one-half that in dogs. To nitrous oxide have been added nitrogen and argon¹⁴⁶ and xenon¹⁴⁷ constituting a group of chemically inert gases which have anesthetic potency. Effectiveness is related to lipid solubility and lends support to the thesis that accumulation of chemically inert substances can produce narcosis.

Eldjarn¹⁰² has investigated the metabolism of antabuse by means of radioactive sulfur and estimates the desired antabuse blood level as 0.5 to 1.0 mg./100 ml. He finds prolonged retention of antabuse (up to 6 days) and recommends downward revision of dosage schedules. Similar recommendations might be drawn from three reports¹⁰³⁻¹⁰⁵ describing more than 14 cases of psychotic episodes during antabuse therapy. All of these responded eventually to discontinuation of the antabuse administration. Giarman, Flick and White¹⁰⁶ advise caution in the use of thiopental in patients undergoing antabuse therapy since they find a marked prolongation of anesthesia in such circumstances.

The mechanism by which barbiturates accomplish their narcotic action remains obscure. The extended publication of the work of Lamson et al.¹⁰⁷ on the potentiation of barbiturate anesthesia by a variety of substances

including glucose and several intermediary metabolites of carbohydrates is very welcome. Langlois and Williams¹⁰⁸ and Richards et al.¹⁰⁹ have extended the list of substances which produce this effect but the latter's findings do not permit them to accept carbohydrate metabolites as the common denominator. Lamson's group tends to relate this effect to altered permeability of the brain through an effect on an ACh-ChE mechanism but so far the data seem no more than suggestive. A possible clue to a biochemical mechanism is provided by Brody and Bain¹¹⁰ whose studies on brain slices *in vitro* with a pyruvate substrate have led them to postulate that "an uncoupling of phosphorylation from oxidation" may be involved. However, Karlsson, Sutherland and Elliott¹¹¹ report that "in the presence of pentobarbital, oxidation of glucose, and not of pyruvate, results in interference with further oxygen uptake." The mechanism of this effect is not known, nor is its significance understood, but it seems to indicate a link of pentobarbital action to glucose rather than to pyruvate oxidation. Wechsler, Dripps and Kety¹¹² report a decrease in cerebral oxygen consumption during thiopental anesthesia, but do not establish whether this is cause or effect of the drug action. Failure of narcotic concentrations of pentobarbital to decrease oxygen consumption of brain tissue *in vivo* is reported by Grenell and Davies,¹¹³ and Westfall¹¹⁴ reports increases in oxygen consumption by brain preparations *in vitro*. Continuing the meticulous work for which their group has become known, Giotti and Maynert¹¹⁵ find data which "support the hypothesis that barbitol is reabsorbed in the renal tubules as the free acid by a process of back-diffusion."

In his analysis of the EEG in barbiturate-induced sleep in man, Wyke¹¹⁶ finds that "as the brain falls asleep it does so piecemeal," exhibiting a serial depression of activity which, however, he does not believe can be explained on the theory of depression of successively lower levels. Kiersey, Bickford and Faulconer¹¹⁷ continuing Bickford's attempts to devise a satisfactory servo-mechanism for anesthesia with the integrated EEG as the controlling factor, have described and classified the EEG patterns produced by thiopental during surgical anesthesia in humans.

Reports appear to be accumulating in support of Isbell's contention that physical dependence on barbiturates can occur. Alexander¹¹⁸ describes hallucinations, tremor, insomnia and occasional convulsions while Hewitt¹¹⁹ presents 12 cases, 3 of them in detail, of psychosis following abrupt termination of barbiturate therapy. Isbell¹²⁰ has resummarized the situation. Fernando¹²⁰ has advanced the interesting though inadequately documented thesis that "the efficiency of the barbiturates as anticonvulsants depends, if not entirely, at least mainly, on their blocking of the action of ACh" and finds a concurrent diminution of ChE activity. He believes the occurrence of convulsions on withdrawal of barbiturates may result from a residual

antiChE action persisting after disappearance of the ACh blocking effect. In connection with a fairly extensive survey of thiobarbiturates, Richards¹²¹ calls attention to a considerable species variation in dominance of convulsive or anticonvulsive effects from compounds which tend to possess both actions. He finds convulsant properties most prominent in rabbits, mixed actions in mice and sedative effects prominent in monkeys. There seems to be a tendency toward reevaluation of the available analeptics with respect to their efficacy in the treatment of acute barbiturate poisoning.

Important developments in the field of analgesia testing are the demonstrations by the Ann Arbor (Irwin et al.)¹²² and the Lexington (Houde and Wikler)^{123, 124} groups that several of the common indices of pain perception used in the determination of analgesic processes in animals are spinal reflexes, integrated to such a large extent subcortically that they cannot reflect possible suprasegmental actions in any simple fashion. However, empirical correlation with clinical action may be practical. Though these reflexes are subject to inhibition by such potent analgesics as morphine and, in some cases, methadone and meperidine, Irwin et al. nevertheless interpret their data to indicate that these analgesics enhance a supraspinal inhibitory mechanism controlling these spinal reflexes. Thus, there may be opposite actions of analgesics on spinal and supraspinal sites. Renewed interest in the Hardy-Wolff-Goodell pain-threshold apparatus should result from the work of Kuhn and Bromiley.¹²⁵ They have taken the significant precautions of randomizing stimulus intensities, so that the subject has no basis for predicting the effect of the next trial, and repeating stimuli around the threshold intensity a sufficient number of times to insure a valid determination. The question whether alteration of pain-threshold or relief of naturally occurring pain is the preferred method of evaluating analgesics still remains. Beecher and his group, the principal proponents of the latter method, have continued their work with an evaluation of intravenous procaine.¹²⁶ They find a slight, but significant relief of pain, but only "at the cost of tremendous side-action liability." They comment that the best results with this drug have been reported in treatment of symptoms which have a large psychic overlay or which are notoriously variable or where the degree of pain is minor, and reiterate their plea for objectivity and the use of controls in investigations of pain. Beecher and co-workers¹²⁷ have extended their studies of analgesics by comparing methadone and levo-iso-methadone with morphine and a placebo in battle casualties in Korea. They are to be commended for making this evaluation according to their usual rigid criteria under the most difficult of circumstances. Winter and Flataker¹²⁸ report diminution in the effectiveness of morphine and methadone by cortisone and corticotropin (ACTH) and enhancement by DCA. They offer an admittedly incomplete explanation of the mechanisms involved but feel their

data indicate a stimulant influence of cortisone on the entire cerebrospinal axis.

Confirmation of Hart's¹²⁹⁻¹³¹ and, later, Unna's¹³² contention that morphine can be antagonized by n-allyl-normorphine has come from several sources. This antagonism between analogues has been extended to include other species as well as other analgesics.¹³³ In man with depressed respiration from morphine or demerol intravenous injection of n-allyl-normorphine results in a two or three-fold increase in respiratory rate and a 200-300 per cent increase in minute volume.¹³⁴ Wikler¹³⁵ has produced drowsiness, day dreams and dysphoria accompanied by autonomic manifestations on subcutaneous administration to post-addicts. These effects, except for the drowsiness, could be abolished by intravenous pentobarbital but only slight reduction could be obtained by intravenous morphine.

Mescaline-induced functional psychosis has been carefully studied by Hoch¹³⁶ who reports the effects in schizophrenics and in controls as well as the reactivation of psychoses by mescaline in patients who had been relieved by psycho-surgery. Fischer et al.^{137, 137a} point out that liver function tests reveal disturbance in most cases of acute schizophrenia and in mescaline intoxications but that in lysergic acid diethylamide intoxications the disturbance of liver functions is less.

TRANSMISSION PHENOMENA AT THE NEUROEFFECTOR JUNCTION

Cholinergic. The diagnostic use of intra-arterial ACh is again advocated. Engback¹³⁸ differentiates motoneuron lesions from myasthenia of muscular origin on the basis of increased sensitivity to ACh of the former and decrease with the latter. The papers on curare, curare-like and anticurare substances are many and in fair agreement. They are well represented in the symposium held at the New York Academy of Sciences.¹ It becomes quite clear particularly through the work of Paton and Zaimis¹⁴⁰ that decamethonium, which exercises a depolarizing action manifesting itself first as an excitation but very soon as a depression, occupies a middle position between curare and the anticurare substances. The papers of Wescoe and Riker¹³⁹ are particularly instructive with respect to the anticurare substances. They have been principally instrumental in the development and characterization of the aromatic ammoniums which are relatively weak competitive inhibitors of ChE's. The antiChE actions of these compounds do not parallel their anticurare activities and in many cases they are depolarizing agents themselves and, in this respect,² resemble ACh and decamethonium.

Under the special circumstances of chronic denervation Jarcho et al.¹⁴¹ are able to detect decamethonium depolarization outside the endplate area. The distinction between d-tubocurarine and decamethonium is brought out again by Lang, Kimura and Unna¹⁴² who demonstrate a complimentary

action between ether and d-tubocurarine but not decamethonium in depressing neuromuscular transmission. Unna and Pelikan¹⁴³ continue their very careful studies in humans and complain "that it was particularly disconcerting to find that two closely related and chemically similar agents, d-tubocurarine and dimethyl-d-tubocurarine, showed as wide and unpredictable variations in potency in different species as those agents whose structures are as dissimilar as those of flaxedil and d-tubocurarine." Marbury et al.,¹⁴⁴ who studied flaxedil in 57 anesthetized surgical patients, bring out the very important point that cumulative effects occur in spite of apparent recovery of respiratory volume between doses. It has long been held by the present reviewers that distribution of ChE per se should also be interpreted from the point of view of protection afforded to the tissue, possible transmitting functions awaiting actual demonstration of ACh accumulation or its effects. Such a view is utilized, in part, by Feldberg⁶ who points out that the demonstrable detrimental effects of too much ACh at skeletal muscle may be the reason for concentration of true ChE in the end-plate region of skeletal muscle without any decrease occurring after the motor nerve degeneration. Ambache¹⁶¹ presents a further analysis of the action of clostridium botulinum toxin which appears to be at cholinergic synapses in the autonomic system, i.e., both sympathetic and parasympathetic (ciliary) ganglia as well as at cholinergic neuroeffector junctions. Holton and Perry¹⁶³ have investigated the possible transmitter responsible for antidromic vasodilatation in the rabbit's ear. Using the sympathectomized ear and a sensitive photoelectric method for recording changes in vasomotor tone, they were able to produce antidromic vasodilatation which was, however, not amenable to an action of atropine, mepyramine or strychnine or to potentiation by eserine although the vasodilatation was depressed by eserine.

Adrenergic. In anxiety occurring spontaneously or stirred up by psychiatric examination in 14 psychiatric patients and 4 controls, Fleetwood¹⁴⁸ is able to detect an adrenaline-like substance in the blood which he believes to be nor-adrenaline on the basis of biologic tests and resistance to ergotamine. Much work has centered about the adrenal medulla. Van Arman¹⁴⁹ after exhausting the epinephrine store of rat adrenals by insulin concludes that the medulla cannot store epinephrine or nor-epinephrine from the blood, significant recovery occurring only by dietary means including complete diet, amino acid mixtures or dihydroxyphenylalanine. West¹⁵⁰ subjects rabbits to insulin and reports that, during the fluctuation in adrenaline content of the adrenal medulla, noradrenaline appeared in small amounts for only a short time and, therefore, concludes that, if it is the precursor, methylation occurs very rapidly. Cats show a high (60 to 89 per cent) noradrenaline content during resting secretion of the adrenal medulla

which according to Kaindl and Von Euler¹⁵¹ does not change on activation by carotid occlusion in vagotomized cats. The whole adrenal medulla is said to contain a very high proportion of noradrenaline, five times the adrenaline content and Burn et al.¹⁵² remark on the similarity to the composition of human pheochromocytomas. The high noradrenaline content of pheochromocytomas is attributed quite logically by Beyer et al.¹⁵³ to an interference with the normal transmethylation process in the synthesis of adrenaline. Some very intriguing calculations have been made by Guyton and Gillespie¹⁵⁴ on the rate of adrenaline secretion and destruction based upon constant infusion experiments in control dogs and those subjected to complete spinal anesthesia. Judging from the amount of adrenaline necessary to sustain a normal level of blood pressure under total spinal anesthesia they estimate the normal rate of adrenaline secretion as 0.45 gamma/kg./minute and that half of the blood pressure sustaining activity of the sympathetic under normal conditions is due to the secretion of adrenaline. Rate of destruction is estimated as approximately 0.6 of the total quantity in the body per minute and the total quantity of active adrenaline under pentobarbital is calculated as 0.71 gamma/kg. In two healthy subjects into whom they infused noradrenaline Von Euler and Luft¹⁵⁵ by comparing urinary excretion to infused material infer that "normally some 0.5-1.0 gamma of 1-noradrenaline per minute reaches the general circulation." In rabbits, injected noradrenaline has not been recovered from the urine in the free state or as an ester.¹⁵⁶ Swan's⁸² and Taylor and Page's⁸³ results illustrating the vasodilation on adrenaline infusion resulting from ganglionic and central inhibitory actions of the adrenaline have been described above. This is quite different from the reversal of adrenaline and ACh effects on perfused vessels of the rabbit's ear ascribed by Burn and Robinson¹⁶² to a local action.

Angiographic evidence convinces Daniel and Prichard¹⁵⁷ that the effects of hepatic nerve stimulation on circulation of the portal blood within the liver are the same as those of intraportal administration of adrenaline. Chalmers and Keele¹⁵⁸ confirm previous findings on the production of sweating in man by intradermal injections of adrenaline and noradrenaline. Since they cannot prevent this by atropine but can stop normal sweat secretion in this fashion, they do not believe that there is an adrenergic component in physiologic sweating. Wescott and Christensen have succeeded in making an isolated preparation of the nictitating membrane smooth muscle which responds *in vitro* in the same fashion as it does *in vivo* to adrenaline and adrenaline-like compounds and to ACh and to DFP.¹⁶⁶

CONDUCTION AND OTHER MEMBRANE PHENOMENA

Roethth¹⁶⁴ has established through inhibition by DFP that a minimum of ChE is essential for a normal light reflex in the rabbit and also that horse

and rabbit optic nerves are capable of exhibiting choline acetylase activities. To quote him in part this is "in itself again not conclusive as evidence for the essentiality of ACh in conduction" but "removes one of the main objections still maintained against Nachmansohn's theory" and again with reference to the DFP "this result, considered as an isolated phenomenon, does not make possible a distinction whether synaptic transmission or axonal conduction is interrupted if the enzyme activity falls to a low level." A hexokinase inhibitor is described in nerve by Abood and Gerard.¹⁶⁵ The effects of dilantin and mesantoin have been tested by Korey¹⁶⁷ on the squid giant axon. The normal nerve is unaffected but the spontaneous firing produced by low calcium is stopped. A number of antihistamines and related compounds tried by Crescitelli and Geissman¹⁶⁸ all produced a conduction block in bull frog sciatic nerves with little or no modification of the resting potential. There was little specificity with relation to the structural features of the compound. Reilly, Whitehouse and Riker¹⁶⁹ find the effects of methyl fluoroacetate on the heart to be primarily on the contractile mechanism with very little alteration of the conductile properties. Thus, they believe the maintenance of membrane function (as indicated by conduction) is relatively little dependent upon oxidative processes.

Ersner, Spiegel and Alexander¹⁷⁰ have obtained favorable results in about half of a series of 37 patients with Ménière's syndrome following transtympanic injection of local anesthetics or alcohol.

Rudin, Fremont-Smith and Beecher¹⁷¹ find that injection of the usual amounts of procaine into the epidural space in dogs results in penetration of the drug through the dura to an extent adequate for depression of spinal cord function. They find concentrations of procaine in the range of 0.1-1.0 mg./cc. adequate to act directly upon the spinal cord as well as on the spinal rootlets. They offer their findings as an alternate explanation of those "accidents" of caudal anesthesia which are ordinarily attributed to penetration of the meninges by the needle. Lorente de Nó¹⁷² describes a gradient of sensitivity to lack of sodium with increasing distance from the cord in the spinal root of the bull frog. He shows that this has no relation to the anatomic distribution of the epineurium but is an expression of the change in properties exhibited by axons depending upon whether they are in the spinal cord or in a nerve trunk. He¹⁷³ also shows that cocaine diffuses through the epineurium "with remarkable rapidity" and that lack of sodium markedly sensitizes nerve fibers to the anesthetic action of cocaine and goes on to suggest that cocaine anesthetizes nerve fibers through the sodium mechanism at the point in the chemical reaction in which sodium participates. His experiments¹⁷⁴ show further that lithium ions can substitute for sodium but ammonium ions cannot. Crescitelli¹⁷⁵ has repeated his experiments on the actions of drugs on unsheathed nerves by using as control resheathed

nerves and concludes that "it is the removal of the sheath which in the intact nerve acts as a barrier, rather than alterations in the properties of the nerve fibers, which is responsible for the observed experimental effects." Using crab nerve, Shanes¹⁷⁶ establishes to his satisfaction that potassium shifts are in the proper direction and of the proper order of magnitude to account for negative and positive after potentials in terms of potassium accumulation or depletion in the extracellular space. Making use of radioisotopic potassium (K^{42}) Keynes¹⁷⁷ is able to establish leakage of potassium from the stimulated crab nerve. From further experiments using radioisotopic sodium (Na^{24}) as well as the K^{42} , he¹⁷⁸ is able to say "there is no doubt that the sodium entry postulated by Hodgkin and Katz¹⁷⁹ does occur and is roughly equal to the leakage of potassium." Since at least 97 per cent of the intracellular potassium could exchange readily with K^{42} , Keynes and Lewis¹⁸⁰ feel that there is no evidence for bound potassium in this nerve. Steinbach¹⁸¹ has done additional work to show that the isolated frog sartorius muscle depleted of potassium and enriched with sodium can actively extrude sodium and consequently take up potassium during recovery in potassium containing solutions.

REFERENCES

- ¹ Curare and anticurare agents. *Ann. New York Acad. Sc.* 54:297, 1951.
- ² Nerve Impulse. Transactions of the Second Conference, Josiah Macy, Jr. Foundation, New York, 1951.
- ³ de Castro, F., Couteaux, R., Baud, C. A., Bauman, J. A., Weber, A., Feldberg, W., Heymans, C., and Bremer, F.: Comptes rendus du colloque sur les transmissions synaptiques, ganglionnaires et centrales. *Arch. internat. physiol.* 59:479, 1951.
- ⁴ Biology of mental health and disease. Milbank Memorial Fund Symposium. New York, Paul B. Hoeber, Inc., 1951.
- ⁵ Feldberg, W.: Gegenwartige problems auf dem gebiet der chemischen ubertagung von nervenwirkungen. (Present problems concerning the chemical transmission of nervous impulses.) *Arch. Exper. Path. u. Pharmacol.* 212:64, 1950.
- ⁶ —: The physiology of neuromuscular transmission and neuromuscular block. *Brit. M.J.* 4713:967, 1951.
- ⁷ Taylor, D. B.: Some basic aspects of the pharmacology of synthetic curariform drugs. *Pharmacol. Rev.* 3:412, 1951.
- ⁸ von Euler, U. S.: The nature of adrenergic nerve mediators. *Pharmacol. Rev.* 3:247, 1951.
- ⁹ Whittaker, V. P.: Specificity, mode of action and distribution of cholinesterases. *Physiol. Rev.* 31:312, 1951.
- ¹⁰ Griffith, H. R.: New anesthetic drugs. *Canad. M.A.J.* 63:533, 1950.
- ¹¹ Brazier, M. A. B.: The Electrical Activity of the Nervous System. New York, The MacMillan Company, 1951.
- ¹² Eccles, J. C.: The Problems of Chemical Transmission at Synapses in the Central Nervous system. Lecture given at Medical Laboratories, Army Chemical Center, Maryland, December 27, 1951.
- ¹³ Marrazzi, A. S.: Electrical studies on the pharmacology of autonomic synapses.

- II. The action of a sympathomimetic drug (epinephrine) on sympathetic ganglia. *J. Pharmacol. & Exper. Therap.* 65:395, 1939.
- ¹⁴ —: The central inhibitory action of adrenaline and related compounds. *Federation Proc.* 2:33, 1943.
- ¹⁵ — and Hart, E. R.: The action of pilocarpine at a cholinergic cerebral synapse. *J. Pharmacol. & Exper. Therap.* 103:353, 1951.
- ¹⁶ — and Hart, E. R.: Cerebral synaptic action of amphetamine and ephedrine compared with that of caffeine. *Federation Proc.* 10:322, 1951.
- ¹⁷ Chang, H. T.: Dendritic potential of cortical neurons produced by direct electrical stimulation of the cerebral cortex. *J. Neurophysiol.* 14:1, 1951.
- ¹⁸ Verzeano, M.: Servo-motor integration of the electrical activity of the brain and its applications to the automatic control of narcosis. *EEG & Clin. Neurophysiol.* 3:25, 1951.
- ¹⁹ Burns, B. D.: Some properties of isolated cortex in the unanesthetized cat. *J. Physiol.* 112:156, 1951.
- ²⁰ McIlwain, H.: Metabolic response *in vitro* to electrical stimulation of sections of mammalian brain. *Biochem. J.* 49:382, 1951.
- ²¹ Koelle, G. B.: The elimination of enzymatic diffusion artifacts in the histochemical localization of cholinesterase and a survey of their cellular distributions. *J. Pharmacol. & Exper. Therap.* 103:153, 1951.
- ²² Sherwood, S. L., Ridley, E., and McCulloch, W. S.: Effects of intraventricular acetylcholine, cholinesterase and related compounds in normal and "catatonic" cats. *Nature, London* 169:157, 1952.
- ²³ Rowntree, D. W., Nevin, S., and Wilson, A. J.: Effects of di-isopropyl-fluorophosphonate in schizophrenia and manic depressive psychosis. *Neurol., Neurosurg. & Psychiat.* 13:47, 1950.
- ²⁴ Sherwood, S. L.: Brain. In press. (Quoted by Sherwood, Ridley and McCulloch.)
- ²⁵ Forster, F. M.: Critical evaluation of the possible role of acetylcholine in epilepsy. *J. Neuropath. & Clin. Neurol.* 1:98, 1951.
- ²⁶ Pickford, M. and Watt, J. A.: A comparison of the effect of intravenous and intracarotid injections of acetylcholine in the dog. *J. Physiol.* 114:333, 1951.
- ²⁷ Chennells, M., Floyd, W. F., and Wright, S.: The action of di-isopropyl-fluorophosphonate on the central nervous system of the cat. *J. Physiol.* 114:107, 1951.
- ²⁸ Funderburk, W. H. and Case, T. J.: The effect of atropine on cortical potentials. *EEG & Clin. Neurophysiol.* 3:213, 1951.
- ²⁹ Robinson, F. and Hughes, R. A.: Effects of adenine compounds on electrocortical activity. *J. Neurophysiol.* 14:387, 1951.
- ³⁰ Sawyer, C. H., Markee, J. E., and Everett, J. W.: Blockade of neurogenic stimulation of the rabbit adenohypophysis by banthine. *Am. J. Physiol.* 166:223, 1951.
- ³¹ Krivoy, W. A., Hart, E. R. and Marrazzi, A. S.: Further analysis of the actions of DFP and curare on the respiratory center. *J. Pharmacol. & Exper. Therap.* 103:351, 1951.
- ³² Heymans, C., Hyde, J. E., and Terp, P.: Action of trihexylphenidyl (artane) and atropine on central synaptic transmission. *Arch. internat. pharmacodyn.* 86:215, 1951.
- ³³ —, Delaunoy, A. L. & Verbeke, R.: Nicotine and cardioinhibitory vagal center. *Arch. internat. pharmacodyn.* 84:221, 1950.
- ³⁴ Morrison, J. L., Heymans, C., Richardson, A. P., and Walker, H. A.: The comparative action of certain ganglionic blocking agents. *Arch. internat. pharmacodyn.* 86:203, 1951.

- ³⁵ Bonnet, V.: p. 579 of reference #3.
- ³⁶ Bernhard, C. G. and Taverner, D.: The action of d-tubocurarine on the mono-synaptic extensor reflex in the cat. *J. Physiol.* 113:23P, 1950.
- ³⁷ McIntyre, A. R., Bennett, A. L., and Hamilton, C.: p. 546 of reference #3.
- ³⁸ Davison, M. H. A.: Mephenesin in tetanus. *Anesthesiology*. 12:120, 1951.
- ³⁹ Boles, T. C. and Smith, J. H.: Mephenesin in treatment of tetanus; results of oral administration in three cases. *J.A.M.A.* 146:1296, 1951.
- ⁴⁰ Funderburk, W. H., King, E. E., and Unna, K. R.: The site of action of benzazoles in the central nervous system. *J. Pharmacol. & Exper. Therap.* 103:343, 1951.
- ⁴¹ Elliott, K. A. C. and Henderson, N.: Factors affecting acetylcholine found in excised rat brain. *Am. J. Physiol.* 165:365, 1951.
- ⁴² McIlwain, H., Anguiano, G., and Cheshire, J. D.: Electrical stimulation *in vitro* of the metabolism of glucose by mammalian cerebral cortex. *Biochem. J.* 50:12, 1951.
- ⁴³ Greig, M. E. and Mayberry, T. C.: The relationship between cholinesterase activity and brain permeability. *J. Pharmacol. & Exper. Therap.* 102:1, 1951.
- ⁴⁴ Keasling, H. H., Featherstone, R. M., Schueler, F. W., and Gross, E. G.: Further observations on the anesthetization of rabbit's cornea by non-surface anesthetics. *Proc. Soc. Exper. Biol. & Med.* 77:31, 1951.
- ⁴⁵ Aird, R. B. and Strait, L.: The mode of action of sodium diphenylhydantoinate (dilantin) in epilepsy. *J. Pharmacol. & Exper. Therap.* 103:136, 1951.
- ⁴⁶ — and Gordan, G. S.: Anticonvulsive properties of desoxycorticosterone. *J.A.M.A.* 145:715, 1951.
- ⁴⁷ Gordan, G. S. and Aird, R. B.: Sublingual desoxycorticosterone for the control of convulsive seizures. *Ciba Clin. Symposia.* 3:57, 1951.
- ⁴⁸ Root, M. A.: Certain aspects of the vasopressor action of pilocarpine. *J. Pharmacol. & Exper. Therap.* 101:125, 1951.
- ⁴⁹ Marrazzi, A. S.: Electrical studies on the pharmacology of autonomic synapses. I. The action of parasympathomimetic drugs on sympathetic ganglia. *J. Pharmacol. & Exper. Therap.* 65:18, 1939.
- ⁵⁰ Ambache, N.: The nicotinic action of substances supposed to be purely smooth-muscle stimulating; effect of BaCl₂ and pilocarpine on the superior cervical ganglion. *J. Physiol.* 110:164, 1949.
- ⁵¹ Carr, E. A. Jr. and Riggs, D. S.: Parasympathomimetic effects of the ethylal of gamma-trimethylammoniumpropanediol iodide (F2268). *J. Pharmacol. & Exper. Therap.* 102:272, 1951.
- ⁵² Chen, G., Portman, R., and Wickel, A.: Pharmacology of 1,1-dimethyl-4-phenylpiperazinium iodide, a ganglion stimulating agent. *J. Pharmacol. & Exper. Therap.* 103:330, 1951.
- ⁵³ Gyermek, L. and Sztanyik, L.: The ganglionic blocking activity of tropeins. *Acta physiol. hung.* 2:41, 1951.
- ⁵⁴ Feldberg, W.: Effects of ganglion-blocking substances on the small intestine. *J. Physiol.* 113:483, 1951.
- ⁵⁵ Ambache, N. and Edwards, J.: Reversal of nicotine action on the intestine by atropine. *Brit. J. Pharmacol.* 6:311, 1951.
- ⁵⁶ — and Rocha e Silva, M.: Analysis of certain interactions of nicotine with bradykinin and histamine. *Brit. J. Pharmacol.* 6:68, 1951.
- ⁵⁷ Margolin, S., Makovsky, A., Spoerlein, M. T., Stephens, I., and Tislow, R.: A new selectively acting parasympathetic blocking agent—N,N-dimethyl-4-pi-

- perdylidene-1,1-diphenylmethane methyl sulfate (Prantal). *J. Pharmacol. & Exper. Therap.* 103:352, 1951.
- ⁵⁸ Paton, W. D. M. and Zaimis, E. J.: Paralysis of autonomic ganglia by methonium salts. *Brit. J. Pharmacol.* 6:155, 1951.
- ⁵⁹ Grob, D. and Harvey, M.: Observation on the effects of the autonomic blocking agent, bis-trimethylammonium pentane dibromide (C_8) in normal subjects and in patients with peripheral vascular disease and hypertension, and comparison with tetraethylammonium chloride. *Bull. Johns Hopkins Hosp.* 87:637, 1950.
- ⁶⁰ Paton, W. D. M. and Zaimis, E. J.: The action of d-tubocurarine and of decamethonium on respiratory and other muscles in the cat. *J. Physiol.* 112:311, 1951.
- ⁶¹ Riker, W. F. Jr. and Wescoe, W. C.: The pharmacology of flaxedil with observations on certain analogs. *Ann. New York Acad. Sc.* 54:30, 1951.
- ⁶² Paton, W. D. M.: p. 433 of ref. #1.
- ⁶³ Doshay, L. J. and Constable, K.: Newer drugs in the treatment of parkinsonism. *Neurology.* 1:68, 1951.
- ⁶⁴ Gitt, J. J., Landau, W. M., and Clare, M. H.: Influence of benadryl upon electromyographic recordings in parkinsonism. *Dis. Nerv. System.* 12:117, 1951.
- ⁶⁵ Moore, M. T.: Benadryl in the treatment of Parkinson's disease. *Neurology.* 1:123, 1951.
- ⁶⁶ Bovet, D. and Longo, V. G.: The action on nicotine-induced tremors of substances effective in parkinsonism. *J. Pharmacol. & Exper. Therap.* 102:22, 1951.
- ⁶⁷ McCawley, E. L., Brookhart, J. M., and Kulasavage, R. J.: Studies on diphenhydramine on the vomiting center. *J. Pharmacol. & Exper. Therap.* 103:354, 1951.
- ⁶⁸ Borison, H. L. and Wang, S. C.: Locus of the central emetic action of cardiac glycosides. *Proc. Soc. Exper. Biol. & Med.* 76:335, 1951.
- ⁶⁹ —: Functional localization of central coordinating mechanism for emesis in cat. *J. Neurophysiol.* 12:305, 1949.
- ⁷⁰ Fairbanks, V. F. and Borison, H. L.: Studies on emetic action of veratrum alkaloids in cats. *J. Pharmacol. & Exper. Therap.* 103:343, 1951.
- ⁷¹ Borison, H. L. and Brizzee, K. R.: Morphology of emetic chemoreceptor trigger zone in cat medulla oblongata. *Proc. Soc. Exper. Biol. & Med.* 77:38, 1951.
- ⁷² Gutner, L. B., Gould, W. J., and Batterman, R. C.: Action of dimenhydrinate (dramamine) and other drugs on vestibular function. *Arch. Otolaryng.* 53:308, 1951.
- ⁷³ Gay, L. N.: Prophylactic and therapeutic control of vestibular disturbances with dimenhydrinate. *J.A.M.A.* 145:712, 1951.
- ⁷⁴ Kerman, E. F.: Dramamine in the prevention and treatment of nausea and vomiting following electroshock therapy. *Dis. Nerv. System.* 12:83, 1951.
- ⁷⁵ Rudolph, C. J., Park, D. D., and Hamilton, C.: Treatment of postanesthesia nausea and vomiting. *J.A.M.A.* 144:1283, 1950.
- ⁷⁶ Wollgast, G. F. and Prockter, W. H.: Dramamine in general surgery. A comparative clinical evaluation. *Am. Surgeon* 17:628, 1951.
- ⁷⁷ Lennox, M. A., Ruch, T. C., and Guterman, B.: The effect of benzedrine on the post-electroshock EEG. *EEG & Clin. Neurophysiol.* 3:63, 1951.
- ⁷⁸ Lundberg, A.: Adrenaline and transmission in a sympathetic ganglion. *Scand. Physiol. Congress. Aarhus VII*:56, 1951.
- ⁷⁹ Bulbring, E. and Burn, J. H.: An action of adrenaline on transmission in sympathetic ganglia, which may play a part in shock. *J. Physiol.* 101:289, 1942.

- ⁸⁰ tum Suden, C., Hart, E. R., Lindenberg, R., and Marrazzi, A. S.: Pharmacologic and anatomic indications of adrenergic neurons participating in synapses at parasymphathetic ganglia (ciliary). *J. Pharm. & Exper. Therap.* 103:364, 1951.
- ⁸¹ DeCastro, F.: pp. 479-514 of ref. #3.
- ⁸² Swan, H. J. C.: Observations on a central dilator action of adrenaline in man. *J. Physiol.* 112:426, 1951.
- ^{82a} Duff, R. S. and Swan, H. J. C.: Further observations on the effect of adrenaline on the blood flow through skeletal muscles. *J. Physiol.* 114:41, 1951.
- ⁸³ Taylor, R. D. and Page, I. H.: Peripheral vasomotor effects of adrenaline and noradrenaline acting upon the isolated perfused central nervous system. *Circulation.* 4:563, 1951.
- ⁸⁴ Heymans, C. de Vleeschhouwer, G. R., and Heuvel-Heymans, G. v. d.: Adrenolytic drug and action of adrenaline and noradrenaline on carotid sinus. *Arch. internat. pharmacodyn.* 85:188, 1951.
- ⁸⁵ Bremer, F.: Les reactions auditives de l'écorce cerebrale. *L'ann. psychol. Vol. jubilaire*:115, 1951.
- ⁸⁶ Chang, H. T.: An observation on the effect of strychnine on local cortical potentials. *J. Neurophysiol.* 14:23, 1951.
- ⁸⁷ Wall P. D. and Horwitz, N. H.: Observations on the physiological action of strychnine. *J. Neurophysiol.* 14:257, 1951.
- ⁸⁸ Frankenhauser, B.: Limitations of method of strychnine neuronography. *J. Neurophysiol.* 14:73, 1951.
- ⁸⁹ Dow, R. S.: The electrical activity of the cerebellum and its functional significance. *J. Physiol.* 94:67, 1938.
- ⁹⁰ Swank, R. L. and Brendler, S. J.: The cerebellar electrogram; effects of anesthesia, analeptics, and local novocaine. *EEG & Clin. Neurophysiol.* 3:207, 1951.
- ⁹¹ Hoff, E. C., Langford, H. G., Vester, J. W., Beckner, W. W., and Thomas, P. R.: Strychnine facilitation of pressor responses evoked from cerebral cortex. *J. Neurophysiol.* 14:167, 1951.
- ⁹² Patterson, J. W. and Mastin, D. W.: Some effects of dehydroascorbic acid on the central nervous system. *Am. J. Physiol.* 167:119, 1951.
- ⁹³ Shideman, F. E. and Procita, L.: Some pharmacological actions of polypropylene glycols of average molecular weight, 400, 750, 1200 and 2000. *J. Pharmacol. & Exper. Therap.* 103:293, 1951.
- ⁹⁴ Webb, J. L. and Elliott, K. A. C.: Effects of narcotics and convulsants on tissue glycolysis and respiration. *J. Pharmacol. & Exper. Therap.* 103:24, 1951.
- ⁹⁵ McLennan, H. and Elliott, K. A. C.: Effects of convulsant and narcotic drugs on acetylcholine synthesis. *J. Pharmacol. & Exper. Therap.* 103:35, 1951.
- ⁹⁶ Chance, M. R. A.: Central nervous function and changes in brain metabolite concentration; characteristic glycogen increment patterns produced by convulsant drugs. *Brit. J. Pharmacol.* 6:1, 1951.
- ⁹⁷ Brink, F. Jr.: p. 124 of ref. #2.
- ⁹⁸ Larrabee, M. G. and Posternak, J. M.: Selective action of anesthetics on synapses and axons in mammalian sympathetic ganglia. *J. Neurophysiol.* 15:91, 1952.
- ⁹⁹ Van Herrevelde, A., Foster, R. J., and Fasman, G. D.: Effect of diphenyl hydantoin (dilantin) on ether and pentobarbital (nembutal) narcosis. *Am. J. Physiol.* 166:718, 1951.
- ¹⁰⁰ Bunker, J. P., Beecher, H. K., Briggs, B. D., Brewster, W. R., and Barnes, B. A.: Metabolic effects of anesthesia. II. A comparison of acid-base equilibrium in

- man and in dogs during ether and during cyclopropane anesthesia. *J. Pharmacol. & Exper. Therap.* 102:62, 1951.
- ¹⁰¹ Morris, L. E., Frederickson, E. L., and Orth, O. S.: Differences in the concentration of chloroform in the blood of man and dog during anesthesia. *J. Pharmacol. & Exper. Therap.* 101:56, 1951.
- ¹⁰² Eldjarn, L.: The metabolism of tetraethyl thiuramdisulphide (antabus, aversan) in man, investigated by means of radioactive sulphur. *Scandinav. J. Clin. & Lab. Invest.* 2:202, 1950.
- ¹⁰³ Gottesfeld, B. H., Lasser, L. M., Conway, E. J., and Mann, N. M.: Psychiatric implications of the treatment of alcoholism with tetraethylthiuram disulfide; a preliminary report. *Quart. J. Stud. Alcohol* 12:184, 1951.
- ¹⁰⁴ Bennett, A. E., McKeever, L. G., and Turk, R. E.: Psychotic reactions during tetraethylthiuramdisulfide (antabuse) therapy. *J.A.M.A.* 145:483, 1951.
- ¹⁰⁵ Martensen-Larsen, O.: Psychotic phenomena provoked by tetraethylthiuram disulfide. *Quart. J. Stud. Alcohol* 12:206, 1951.
- ¹⁰⁶ Giarman, N. J., Flick, F. H., and White, J. M.: Prolongation of thiopental anesthesia in the mouse by premedication with tetraethylthiuram disulfide ("antabuse"). *Science*, 114:35, 1951.
- ¹⁰⁷ Lamson, P. D., Greig, M. E., and Hobdy, C. J.: Modification of barbiturate anesthesia by glucose, intermediary metabolites and certain other substances. *J. Pharmacol. & Exper. Therap.* 103:460, 1951.
- ¹⁰⁸ Langlois, K. and Williams, L.: Action of adenosinetriphosphate and adenosine-monophosphate on thiopental sodium-glucose narcosis. *J. Pharmacol. & Exper. Therap.* 103:351, 1951.
- ¹⁰⁹ Richards, R. K., Bertcher, E. L., and Taylor, J. D.: Effect of various solutions upon barbiturate anesthesia. *J. Pharmacol. & Exper. Therap.* 103:359, 1951.
- ¹¹⁰ Brody, T. M. and Bain, J. A.: Effect of barbiturates on oxidative phosphorylation. *Proc. Soc. Exper. Biol. & Med.* 77:50, 1951.
- ¹¹¹ Karlsson, J. L., Sutherland, V. C., and Elliott, H. W.: Delayed arrest of rat brain slice respiration caused by pentobarbital during the metabolism of glucose. *J. Pharmacol. & Exper. Therap.* 103:1, 1951.
- ¹¹² Wechsler, R. L., Dripps, R. D., and Kety, S. S.: Blood flow and oxygen consumption of the human brain during anesthesia produced by thiopental. *Anesthesiology* 12:308, 1951.
- ¹¹³ Grenell, R. G. and Davies, P. W.: Effect of nembutal on the *in vivo* rate of oxygen consumption of the cerebral cortex. *Tr. Am. Neurol. A.* 175:105, 1950.
- ¹¹⁴ Westfall, B. A.: Effects of pentobarbital amobarbital and barbital on oxygen consumption of brain slices. *J. Pharmacol. & Exper. Therap.* 101:163, 1951.
- ¹¹⁵ Giotti, A. and Maynert, E. W.: The renal clearance of barbital and the mechanism of its reabsorption. *J. Pharmacol. & Exper. Therap.* 101:296, 1951.
- ¹¹⁶ Wyke, B. D.: Electrical activity of the human brain during artificial sleep. 2. Regional differentiation of response to barbiturate sedation. *J. Neurol., Neurosurg. & Psychiat.* 14:137, 1951.
- ¹¹⁷ Kiersey, D. K., Bickford, R. G., and Faulconer, A. Jr.: Electroencephalographic patterns produced by thiopental sodium during surgical operations; description and classification. *Brit. J. Anaesth.* 23:141, 1951.
- ¹¹⁸ Alexander, E. J.: Withdrawal effects of sodium amytal. *Dis. Nerv. System* 12:77, 1951.
- ¹¹⁹ Hewitt, R. T.: A psychosis with barbiturate withdrawal. *J. Nerv. & Ment. Dis.* 112:526, 1950.

- 120 Fernando, H. E.: Blocking of action of acetylcholine by barbiturates. *Science*. 115:43, 1952.
- 121 Richards, R. K.: Studies on "convulsive" thiobarbiturates. *Current Res. in Anesth. & Analg.* 30:348, 1951.
- 122 Irwin, S., Houde, R. W., Bennett, D. R., Hendershot, L. C., and Seevers, M. H.: The effects of morphine methadone and meperidine on some reflex responses of spinal animals to nociceptive stimulation. *J. Pharmacol. & Exper. Therap.* 101:132, 1951.
- 123 Houde, R. W. and Wikler, A.: Delineation of the skin-twitch response in dogs and the effects thereon of morphine, thiopental and mephensin. *J. Pharmacol. & Exper. Therap.* 103:236, 1951.
- 124 Houde, R. W., Wikler, A., and Irwin, S.: Comparative actions of analgesic, hypnotic and paralytic agents on hind-limb reflexes in chronic spinal dogs. *J. Pharmacol. & Exper. Therap.* 103:243, 1951.
- 125 Kuhn, R. A. and Bromiley, R. B.: Human pain thresholds determined by the radiant heat technique and the effect upon them of acetylsalicylic acid, morphine sulfate and sodium phenobarbital. *J. Pharmacol. & Exper. Therap.* 101:47, 1951.
- 126 Keats, A. S., D'Alessandro, G. L., and Beecher, H. K.: A control study of pain relief by intravenous procaine. *J.A.M.A.* 147:1761, 1951.
- 127 Beecher, H. K., Deffer, P. A., Fink, F. E., and Sullivan, D. B.: Field use of methadone and levo-iso-methadone in a combat zone (Hamhung-Hungnam, North Korea). *U. S. Armed Forces M. J.* 2:1269, 1951.
- 128 Winter, C. W. and Flataker, L.: The effect of cortisone, desoxycorticosterone, and adrenocorticotrophic hormone upon the responses of animals to analgesic drugs. *J. Pharmacol. & Exper. Therap.* 103:93, 1951.
- 129 Hart, E. R.: N-allylnorcodeine and n-allylnormorphine, two antagonists to morphine. *J. Pharmacol. & Exper. Therap.* 72:19, 1941.
- 130 —: Further observations on the antagonistic actions of n-allylnormorphine against morphine. *Federation Proc.* 2:82, 1943.
- 131 — and McCawley, E. L.: The pharmacology of n-allylnormorphine as compared with morphine. *J. Pharmacol. & Exper. Therap.* 82:339, 1944.
- 132 Unna, K.: Antagonistic effect of n-allylnormorphine upon morphine. *J. Pharmacol. & Exper. Therap.* 79:27, 1943.
- 133 Smith, C. C., Lehman, E. G., and Gilfillan, J. L.: Antagonistic action of n-allylnormorphine upon the analgetic and toxic effects of morphine, methadone derivatives and isonipecaine. *Federation Proc.* 10:335, 1951.
- 134 Eckenhoff, J. E., Elder, J. D., and King, B. D.: The effect of n-allyl normorphine in treatment of opiate overdose. *Proc. Physiol. Soc. Philadelphia.* 26:18, 1950-1951.
- 135 Wikler, A.: Effects of large doses of n-allylnormorphine on man. *Federation Proc.* 10:345, 1951.
- 136 Hoch, P. H.: Experimentally produced psychoses. *Am. J. Psychiat.* 107:607, 1951.
- 137 Fischer, R., Georgi, F., and Weber, R.: Psychophysische Korrelationen. VIII. Modellversuche zum Schizophrenie-problem: Lyseraurediaethylamid und Mezcalin. (Psychophysical correlations. VIII. Experimental tests in schizophrenia; lysergic acid diethylamide and mescaline.) *Schweiz. med. Wchnschr.* 81:817, 1951.
- 137a —: Psychophysische Korrelationen; VIII. Modellversuche zum Schizophrenie problem Lyseraurediaethylamid und Mezcalin. (Psychophysical correlations.

- VIII. Experimental tests in schizophrenia: lysergic acid diethylamide and mescaline.) Schweiz. med. Wchnschr. 81:837, 1951.
- ¹³⁸ Engbaek, L.: Acetylcholine sensitivity in diseases of the motor system with special regard to myasthenia gravis. EEG & Clin. Neurophysiol. 3:155, 1951.
 - ¹³⁹ Wescoe, W. C. and Riker, W. F. Jr.: The pharmacology of anti-curare agents. Ann. New York Acad. Sc. 54:438, 1951.
 - ¹⁴⁰ Paton, W. D. M. and Zaimis, E. J.: p. 347 of ref. #1.
 - ¹⁴¹ Jarcho, L. W., Berman, B., Eyzaguirre, C., and Lilienthal, J. L. Jr.: Curarization of denervated muscle. Ann. New York Acad. Sc. 54:337, 1951.
 - ¹⁴² Lang, D. A., Kimura, K. K., and Unna, K. R.: The combination of skeletal muscle relaxing agents with various central nervous system depressants used in anesthesia. Arch. internat. pharmacodyn. 85:257, 1951.
 - ¹⁴³ Unna, K. R. and Pelikan, E. W.: Evaluation of curarizing drugs in man. VI. Critique of experiments on unanesthetized subjects. P. 480 of ref. #1.
 - ¹⁴⁴ Marbury, B. E., Artusio, J. F. Jr., Wescoe, W. C. and Riker, W. F. Jr.: The effects of a synthetic curare-like compound, the tri-iodo salt of tris (triethylaminoethoxy) 1, 2, 3 benzene (Flaxedil), on the anesthetized surgical patient. J. Pharmacol. & Exper. Therap. 103:280, 1951.
 - ¹⁴⁵ Suden, C. and Marrazzi, A. S.: Synaptic inhibitory action of adrenaline at parasympathetic synapses. Federation Proc. 10:138, 1951.
 - ¹⁴⁶ Marshall, J. M.: Nitrogen narcosis in frogs and mice. Am. J. Physiol. 166:699, 1951.
 - ¹⁴⁷ Cullen, S. C. and Gross, E. G.: The anesthetic properties of xenon in animals and human beings, with additional observations on krypton. Science. 113:580, 1951.
 - ¹⁴⁸ Fleetwood, M. F.: Determination of adrenergic substance in blood related to anxiety. Identification as nor-adrenaline. Am. J. Physiol. 166:314, 1951.
 - ¹⁴⁹ Van Arman, C. G.: Aminoacids and amines as precursors of epinephrine. Am. J. Physiol. 164:476, 1951.
 - ¹⁵⁰ West, G. B.: Insulin and the suprarenal gland of the rabbit. Brit. J. Pharmacol. 6:289, 1951.
 - ¹⁵¹ Kaindl, F. and Von Euler, U. S.: Liberation of nor-adrenaline and adrenaline from the suprarenals of the cat during carotid occlusion. Am. J. Physiol. 166:284, 1951.
 - ¹⁵² Burn, J. H., Langemann, H., and Parker, R. H. O.: Noradrenaline in whale suprarenal medulla. J. Physiol. 113:123, 1951.
 - ¹⁵³ Beyer, K. H., Ross, C. A., Wiebelhaus, V. D., Waller, W. S. and Schuchardt, G. S.: Vasopressor components of pheochromocytomas. Ann. Int. Med. 35:117, 1951.
 - ¹⁵⁴ Guyton, A. C. and Gillespie, W. M. Jr.: Constant infusion of epinephrine: rate of epinephrine secretion and destruction in the body. Am. J. Physiol. 165:319, 1951.
 - ¹⁵⁵ Von Euler, U. S. and Luft, R.: Noradrenaline output in urine after infusion in man. Brit. J. Pharmacol. 6:286, 1951.
 - ¹⁵⁶ Fischer, P. and Lecomte, J.: Excretion d'arterenol libre dans les urines du lapins non anesthésié. (Excretion of free arterenol in the urine of a non-anesthetized rabbit.) Arch. internat. physiol. 58:358, 1950.
 - ¹⁵⁷ Daniel, P. M. and Prichard, M. M. L.: Effects of stimulation of the hepatic nerves and of adrenaline upon the circulation of the portal venous blood within the liver. J. Physiol. 114:538, 1951.
 - ¹⁵⁸ Chalmers, T. M. and Keele, C. A.: Physiological significance of the sweat response to adrenaline in man. J. Physiol. 113:9, 1951.
 - ¹⁵⁹ Isbell, H.: Treatment of barbiturate addiction. Postgrad. Med. 9:256, 1951.
 - ¹⁶⁰ Ellis, S. and Rasmussen, H.: The atropine-fast nicotine stimulation of the rabbit's

- intestine and of the muscularis mucosae of the dog's intestine. *J. Pharmacol. & Exper. Therap.* 103:259, 1951.
- 161 Ambache, N.: A further survey of the action of clostridium botulinum toxic upon different types of autonomic nerve fibre. *J. Physiol.* 113:1, 1951.
 - 162 Burn, J. H. and Robinson, J.: Reversal of the vascular response to acetylcholine and adrenaline. *Brit. J. Pharmacol.* 6:110, 1951.
 - 163 Holton, P. and Perry, W. L. M.: On the transmitter responsible for antidromic vasodilatation in the rabbit's ear. *J. Physiol.* 114:240, 1951.
 - 164 de Roetth, A. Jr.: Role of acetylcholine in nerve activity. *J. Neurophysiol.* 14:55, 1951.
 - 165 Aboud, L. G. and Gerard, R. W.: A hexokinase inhibitor in nerve. *Proc. Soc. Exper. Biol. & Med.* 77:438, 1951.
 - 166 Wescott, W. C. and Christensen, H. E.: Response of the isolated nictitating membrane (cat). *Am. J. Physiol.* 167:836, 1951.
 - 167 Korey, S. R.: Effect of dilantin and mesantoin on the giant axon of the squid. *Proc. Soc. Exper. Biol. & Med.* 76:297, 1951.
 - 168 Crescitelli, F. and Geissman, T. A.: Certain effects of antihistamines and related compounds on frog nerve fibers. *Am. J. Physiol.* 164:509, 1951.
 - 169 Reilly, J. F., Whitehouse, W. C., and Riker, W. F. Jr.: The effect of methyl fluoroacetate on the papillary muscle of the cat. *J. Pharmacol. & Exper. Therap.* 103:359, 1951.
 - 170 Ersner, M. S., Spiegel, E. A., and Alexander, M. H.: Transtympanic injection of anesthetics for the treatment of Meniere's syndrome. *Arch. Otolaryng.* 54:43, 1951.
 - 171 Rudin, D. O., Fremont-Smith, F. K., and Beecher, H. K.: Permeability of dura matter to epidural procaine in dog. *J. Appl. Physiol.* 3:388, 1951.
 - 172 Lorente de Nó, R.: On the existence of a gradient of sensitivity to the lack of sodium in the spinal roots of the bullfrog. *J. Gen. Physiol.* 35:183, 1951.
 - 173 —: On the effect of cocaine upon sodium-deficient frog nerve. *J. Gen. Physiol.* 35:203, 1951.
 - 174 —: On the effect of ammonium and lithium ions upon frog nerve deprived of sodium. *J. Gen. Physiol.* 35:227, 1951.
 - 175 Crescitelli, F.: Nerve sheath as a barrier to the action of certain substances. *Am. J. Physiol.* 166:229, 1951.
 - 176 Shanes, A. M.: Potassium movement in relation to nerve activity. *J. Gen. Physiol.* 34:795, 1951.
 - 177 Keynes, R. D.: The leakage of radioactive potassium from stimulated nerve. *J. Physiol.* 113:99, 1951.
 - 178 —: The ionic movements during nervous activity. *J. Physiol.* 114:119, 1951.
 - 179 Hodgkin, A. L. and Katz, B.: The effect of sodium ions on the electrical activity of the giant axon of the squid. *J. Physiol.* 108:37, 1949.
 - 180 Keynes, R. D. and Lewis, R. P.: The resting exchange of radioactive potassium in crab nerve. *J. Physiol.* 113:73, 1951.
 - 181 Steinbach, H. B.: Sodium extrusion from isolated frog muscle. *Am. J. Physiol.* 167:284, 1951.

II. NEUROLOGY

CHAPTER 6

Clinical Neurology

By JOSEPH C. YASKIN, M.D. AND CHARLES RUPP, M.D.

THE advances in clinical neurology comprise chiefly recognition and treatment of infections of the nervous system, and the investigation and therapy of some of the vascular and degenerative diseases. Currently, there is a wholesome trend to correlate the advances in internal medicine in the study and treatment of neurologic disease.

INFECTIONS OF THE NERVOUS SYSTEM

Tuberculous Meningitis

Before the advent of treatment with streptomycin, tuberculous meningitis had been uniformly fatal. It is still a common disease, although it is now more common in other parts of the world than in the United States. It is not surprising, therefore, that a great deal of attention has been paid to the management of patients affected with tuberculous meningitis, and that there are many excellent reports from all over the world dealing with the treatment, morbidity and mortality, and complications of treatment, of this disease. It may be well to stress that treatment with streptomycin and other preparations has modified the course of tuberculous meningitis just as the various forms of antiluetic treatment modify the course of neurosyphilis.

Early Diagnosis of Tuberculous Meningitis. With the advent of hopeful therapy, much emphasis must be placed on early diagnosis so that relatively adequate methods of treatment can be instituted. The early diagnosis of tuberculous meningitis is sometimes extremely difficult. In the presence of known tuberculosis elsewhere in the body, evidences of meningeal irritation are highly suggestive, but not conclusive, of tuberculous infection of the meninges. Even with painstaking study of the cerebrospinal fluid, one is often unable to demonstrate the tubercle bacillus, which is the only accurate

means of establishing an etiologic diagnosis. The number and character of the white cells, the reduction of chlorides and sugar, formation of a pellicle, and the various other tests evolved are often not too convincing in establishing a definite diagnosis. Thus, Van Zeben¹ presents pathologic and clinical data on a number of cases of miliary tuberculosis in support of the hypothesis that a tuberculous inflammation of the meninges is already present before the typical abnormalities are detectable in the CSF. Attention is drawn to the opinion of French clinicians that these patients must be treated as promptly and intensively as possible with intrathecal and intramuscular injections of streptomycin, if they are to be given the best and most reliable chance of recovery. In cases where no signs of tuberculous infection are to be found elsewhere in the body, it may be very difficult to arrive at the correct diagnosis. In one case, valuable supporting evidence was obtained by means of isolated ventricle-filling by the method of Ziedses des Plantes. Where doubt exists as to the diagnosis, it is better not to institute treatment, but to await further developments with the patient under strict clinical observation. This is preferable to starting a treatment which may sooner or later have to be suspended on account of the risks involved.

To facilitate the early diagnosis of tuberculous meningitis, a number of old and new studies have been instituted. Thus, Portella² found the tryptophan test of CSF positive in 38 cases, of which 32 were positive for tubercle bacilli. On treatment with streptomycin, the reaction gradually diminished in cases progressing favorably, finally becoming negative. In cases running an unfavorable course, tryptophan reaction remained strongly positive. ⁽³⁾

The approach to an early diagnosis of tuberculous meningitis is being made by many investigators through chemical studies of the cerebrospinal fluid, liver biopsy and encephalography. Urban³ studied the potassium and sodium content of the cerebrospinal fluid in meningitis; Tapie et al.⁴ the chloride content and Ewerbeck⁵ the electrophoresis of the serum proteins in tuberculous meningitis and miliary tuberculosis before and after streptomycin therapy. Van Beek et al.⁶ investigated the aspiration liver biopsy in the early diagnosis of tuberculous meningitis. Liver biopsies were made in 11 of 12 cases of tb meningitis (five confirmed bacteriologically). In all cases, serial sections of the biopsy material showed tubercle structures and in five tb bacilli could be cultured from the material. These cases showed radiologic evidence of hematogenous pulmonary tuberculosis. In two cases with a diagnosis of tuberculous meningitis based on clinical and cerebrospinal fluid signs, but without evidence of pulmonary lesions, tubercle structures (negative cultures) were seen in the liver. In two cases in which the diagnosis of tuberculous meningitis from clinical and cerebrospinal fluid signs were doubtful, the liver showed tubercle structures from which no tubercle bacilli could be cultured. These tubercle structures (epithelioid

cell granulomas) are, however, not typical of tb but may also be found in Besnier-Boeck-Schaumann disease, Bang's disease, leprosy, malignant granuloma, berylliosis and glandular fever.

Aubry et al.⁷ found latent tuberculous meningitis in the course of encephalography. Space precludes mention of several antigen antibody reaction tests and allied studies which, at the present time, have not reached clinical usefulness.

Fouguet⁸ suggests that the slightest abnormality of the cerebrospinal fluid during treatment of miliary tuberculosis or in the course of a primary infection should be regarded as possible evidence of incipient tuberculous meningitis. Since spontaneous regression is extremely rare, intensive intrathecal therapy is recommended. He points out that in children in whom tuberculosis allergy has long been established, other forms of leukocytic meningitis must be very carefully considered.

It has become increasingly clear that latent tuberculosis, especially in the young, may be precipitated by other infections, and possibly by various types of allergic reactions. In this connection, Auersbach and Von Bergmann⁹ report that among 18 patients treated for tuberculous meningitis, there were four in whom the disease developed after immunization against typhoid. Two of the patients were children aged 6 and 3 years, and two were young women aged 16 and 18 years. The meningitis became manifest between 12 days and 8 weeks after the typhoid immunization. Three of the patients died and necropsy revealed a primary caseated tuberculous lesion. In three, the existence of tuberculosis was not known when typhoid immunization was performed but two were known to be allergic to tuberculin and one had had pleurisy three months before. It is stressed that children and adolescents should not be immunized against typhoid unless the result of their tuberculin test is known. Typhoid immunization should not be performed if the tuberculin test is positive or if there are clinical and roentgenologic signs of an active tuberculous process. Immunization against typhoid must be avoided for four years after the primary tuberculous infection.

Treatment of Tuberculous Meningitis. At the present time the chief agents used in the treatment of tuberculous meningitis are streptomycin, para-amino-salicylic acid, streptokinase, promizole, tuberculin, and thiosemicarbazone. The routes of administration employed are oral, subcutaneous, intramuscular and intrathecal. There is no uniformity of opinion regarding the relative value of the various agents used, of the dosage or of the preferred routes of administration. However, there is a growing conviction that the most useful agent is streptomycin, and there is some tendency toward standardization of the dosage and the duration of the treatment.

Perry¹⁰ analyzed 163 consecutive cases of tuberculous meningitis in chil-

dren. One hundred and forty-five patients who were only treated symptomatically died. Forty-eight per cent were under two years, 19 per cent were two to four years and 33 per cent, four to fifteen years at the onset of the disease. The duration of life of 29 untreated cases of miliary tuberculosis from the onset of symptoms to death averaged 50 days, with a range of 7 to 200 days. In 123 untreated cases of tuberculous meningitis, the average duration of life from the first meningitis symptoms to death was 20 days, with an extreme range of 3 to 62 days. Caseous tuberculous foci antedating the meningitis were demonstrated in the central nervous system in 27 out of 70 cases in which a careful pathologic examination was made. Hydrocephalus was found in 25 out of 80 brains examined and tended to appear early in the course of the disease.

Lincoln and Kirmse¹¹ treated 21 children between the ages of 9 months and eleven years with tuberculous meningitis with streptomycin and promizole. They received 1 gm. of streptomycin daily intramuscularly. Streptomycin was also given intrathecally once daily in 0.1 gm. doses until toxic symptoms or mechanical difficulties arose, the dosage was then reduced to 0.05 gm. daily or every two days until a total of 40 intrathecal injections had been given. Promizole was given by mouth four times daily in amounts sufficient to obtain blood concentrations of 1 to 3 mg. per 100 cc. Sixteen patients survived. Three of these relapsed and one subsequently died. There was little evidence of toxic reactions to promizole except for cyanosis and slight thyroid enlargement. Ataxia was the most common toxic reaction to streptomycin. Early recognition and intensive intrathecal therapy are important factors in survival. The location of the lesion, the sensitivity of the micro-organisms, and possibly the age of the patient are important in the prognosis. Four of the five fatalities were under 14 months of age and in a moderate to far advanced stage of the disease. Combined streptomycin and promizole therapy appears to have improved the results and is worthy of more extensive clinical trial.

Russell and MacArthur¹² gave streptomycin to 33 children with tuberculous meningitis. Experience suggests that long intensive intrathecal treatment is unnecessary. Eighteen of the children are dead; ten alive and well, and five alive but disabled. The prognosis is relatively good in patients treated at an early stage of the disease, when the child is over two years of age, and when a "snowstorm" roentgenogram of the lung and choroidal tubercles is absent.

MacCarthy and Mann¹³ treated 43 children with tuberculous meningitis with streptomycin. The period of observation ranged from one year and four months to two years and eight months. All except two of the children were less than seven years of age. The diagnosis was proved bacteriologically in 40 cases. It was the author's impression that the initial response

to therapy depends on a combination of several factors besides streptomycin—age, mechanical obstruction of the cerebrospinal pathways, early diagnosis, innate resistance to tuberculosis and perhaps virulence of the bacillus—and is not greatly influenced by the manner of treatment at the start. The proportion of recoveries will depend much more on the number of initially responsive cases than on the particular rhythm of treatment. In cases showing an initial response to treatment, the shortest road to full recovery seems to be a three-months' course of combined intramuscular and intrathecal streptomycin with not less than 50 intrathecal injections followed by intramuscular treatment until the spinal fluid has been normal on two occasions over a period of three months. A high proportion of full recoveries can be obtained by giving a much shorter course of combined treatment with rest periods (plus intramuscular continuation treatment) provided this is repeated wherever the spinal fluid response is inadequate or recrudescence threatens. However, this method is liable to extend the treatment for well over a year and cannot be recommended.

Smith and Vollum¹⁴ report on 42 patients in whom treatment was begun before October, 1948. In patients with decerebrate rigidity improvement was never seen. During streptomycin treatment, especially in the first weeks, high and fluctuating cell counts and peaks in the protein content are seen due to the liberation of tuberculin in the CSF. Intrathecal injections of 0.75–7.5 μ g. PPD were given to 5 subjects in whom the Mantoux test was negative to 0.1 ml. O.T. 1/100. In no case did any clinical disturbance or cellular and protein response occur. Several times in different subjects and also several times in the same subject, PPD in doses of 0.00375–3.75 μ g. was given intrathecally in subjects with a positive skin reaction to 0.1 ml. O.T. 1/100–1/1,000, but without meningitis. This produces fever, vomiting, pleocytosis and a rise in protein in the CSF. CSF collected during the first few weeks of streptomycin therapy and injected into the skin after Seitz filtration gives no reaction. The result of intradermal injections of CSF collected and filtered 24 hours after an intrathecal injection of PPD is also negative in tuberculin-sensitized subjects. A child with tb meningitis with miliary tb which appeared to be in a hopeless spastic paralyzed condition, was injected intrathecally with minute amounts of PPD two and one-half months after the beginning of the streptomycin treatment. A severe clinical reaction was produced when 7.5 μ g. PPD was injected into the ventricle. (There was fever, vomiting and high intracranial pressure; the upper limbs became as in the classical decerebrate state.) There was a rise of cell-count and protein content in the CSF. Several further injections of 0.75 μ g. PPD were given for four months intracisternally and the dosage was gradually increased. The clinical condition improved gradually. One year after the beginning of the PPD injections

the patient was a fat, healthy looking boy who could walk holding on to someone's hand. The CSF was normal. His vocabulary was still very limited and there were no abnormal neurologic signs except a mild flexion contracture of the right hip and knee.

The second patient, who had also very severe reactions after the intrathecal injections of PPD, is free from all neurologic and mental signs and symptoms and the CSF is approaching normal.

A third patient had a complete decerebrate rigidity when the intrathecal injections were begun. She died 23 weeks later. She showed a sustained objective improvement, though this never amounted to a useful recovery. At necropsy, no exudate was seen macroscopically surrounding the brain stem. Microscopy showed several small foci of tb granulation tissue in the cisterna interpeduncularis and one large focus lying beside the left optic nerve. Intrathecal injections of PPD are potentially extremely dangerous. The severity of the reaction is to some extent unpredictable. Bifrontal burrholes must be made before the injections are given.

Seven other cases are still under treatment. The scheme of treatment in use at present is as follows: On admission, 0.1 ml. O.T. 1/1,000 is injected intradermally. Bifrontal burrholes are made. If the Mantoux test is strongly positive, 0.5 ml. of a 1,000-fold dilution of a solution containing 7.5 μ g. PPD per ml. is injected intrathecally and this amount is doubled every other day until a reaction is obtained. If the Mantoux is weakly positive, 1.0 ml. of the 1,000-fold dilutions is injected and the dose is a first trebled or even quadrupled every other day, depending on the strength of the Mantoux reaction. Once a reaction is obtained, the same dose is repeated. From then on the size and timing of each injection is decided on according to the severity of the last reaction (every third or fourth day). The dose is gradually increased as the patient becomes more tolerant of the injections.

Dubois-Manne¹⁵ reports that of 109 patients whose treatment was started more than two years ago, 38 are alive (19 whose treatment was stopped more than one year ago and 19 more than two years ago). The diagnosis was confirmed bacteriologically in 103 of the 109 cases. Of the 38 survivors, 31 have had no sequelae except slight deafness in a few cases. Thirteen patients with a bacteriologically confirmed diagnosis have been without treatment for more than two years. All are leading normal lives again. The mortality in the first months of treatment is determined chiefly by the stage of the disease at which treatment is started. Of 76 patients treated early, none died in the first month; of 99 treated late, 51 died in the first month. The chance of relapse does not depend on the stage at which treatment is started. Relapses were less frequent in cases whose treatment (intrathecal and intramuscular) was prolonged and supplemented by chemotherapeutics. Hydrocephalus may be due to block of the basal cisterns

or to hypersecretion of CSF. The latter is seen chiefly in the first weeks of treatment when the inflammation is still acute. Permanent drainage of the ventricle for 10 to 12 days is then often successful and without danger. If this does not help, neurosurgery must be undertaken. In tb meningitis, the glucose content of the ventricular CSF is higher than that of the lumbar CSF. With clinical improvement these differences become smaller. Tubercle bacilli were cultured from the (otherwise normal) CSF in 3 of 177 cases of miliary tuberculosis. One of these patients recovered. The bacillus was found in the normal CSF of an infant with a primary infection. Three months later this patient had no clinical manifestations whatever, but the CSF was abnormal and again contained tubercle bacilli. In another infant with severe primary infection and bone tb, the CSF was positive in the guinea-pig test. The CSF was slightly abnormal. This child was treated with streptomycin intramuscularly only. No clinical signs of meningitis appeared.

Gonin et al.¹⁶ treated 62 patients with tuberculous meningitis with streptomycin; 37 were adults, 25 children. Twenty adults and nine children died. Ten adults and thirteen children were cured and stabilization resulted in five adults and two children. The remaining three patients could not be followed. The more favorable prognosis in children and the higher mortality in adults may be accounted for by a greater incidence of meningitis secondary to progressive visceral tuberculosis. Spinal fluid chloride and sugar levels were of value in diagnosis and in control of the course of the disease. Inoculation and cultures were frequently negative. Three to four grams of streptomycin in adults and two to three grams in children were given by the intramuscular route for two weeks. Intraspinal injections were given for 25 to 30 days with a daily dose of 100–150 mg. in adults. General treatment with streptomycin should be continued with doses of 1.5 to 2 gm. daily for one month and with doses of 1 to 1.5 gm. for several months. Best results were obtained in patients treated for 18 months. Six to seven months of treatment are necessary to obtain stabilization. Recurrence of activity at that time is not rare, the occasionally favorable course of these recurrences and of recurrences long after treatment has been discontinued, is proof that resistance to streptomycin is not the cause of therapeutic failure.

Intracranial hypertension, meningeal block and cerebral involvement occurred in seven cases. The early occurrence of intracranial hypertension is a contraindication to surgical intervention.

Bertoye et al.¹⁷ gave streptomycin to 34 children, eight of whom were infants, because of tuberculous meningitis. Twelve received streptomycin by the intramuscular route alone; the others received the drug both intrathecally and intramuscularly. Nineteen patients died, eight recovered. Six

are still under treatment with, so far, good results in four and unsatisfactory results in two. Only one of the eight infants recovered. For better results with streptomycin therapy, it seems imperative to continue the drug intramuscularly for more than eight months and to combine it with intrathecal injections for prolonged periods. Repeated courses of 30 to 45 intrathecal injections should be given if necessary.

Chaptal, Brunel et al.¹⁸ gave streptomycin to 50 children with tuberculous meningitis. Twenty-six children died during treatment. At present, 19 are considered cured. One to two gm. of the drug were given daily until clinical and biologic recovery was maintained for two months after the spinal fluid had been restored to normal. Poor results were obtained when the drug was given by the intramuscular route alone and additional intraspinal administration is considered indispensable. In 18 of the 24 therapeutic failures, treatment was begun after the 10th day. Intracranial hypertension was the cause of death in 16 cases. Neurosurgical treatment should, therefore, be frequently combined with medical treatment. The duration of treatment in the surviving cases ranged from 10½ months to 23 months, and one to twelve months have passed since treatment was discontinued. Deafness resulted in four patients.

Rossi¹⁹ reports on 43 children with tuberculous meningitis who were treated with streptomycin during a period of three years by three methods. All seven children who were given large doses of the drug died. Five of seven given small doses at long intervals for a short period also died. Eighteen of twenty-nine given small doses for a long period either recovered or were considerably improved. At present, 1 to 2 mg. of the drug per kilo of body weight is given intrathecally once or twice daily by intralumbar and suboccipital injection alternately. The dose is reduced during the following weeks to 1 mg. per day with one daily puncture. Three weekly injections with the same dose are given during the second month and two a week during the third month. This regimen is maintained until the spinal fluid returns to normal. Suboccipital injections are given exclusively if the albumin level appears to be more than 10 per cent higher in lumbar than suboccipital puncture. Thirty to 40 mg. per kilo of body weight is given intramuscularly for one month, and this dosage is then reduced to 20 to 30 mg. Combined treatment with 0.3 to 0.5 gm. of para-aminosalicylic acid per kilo of body weight daily is recommended with rest intervals every third or fourth day.

Choremis, Zervos et al.²⁰ used streptomycin in the treatment of 132 children between the ages of 12 months and 15 years; 113 with simple tuberculous meningitis and 19 with tuberculous meningitis combined with miliary tuberculosis. Combined intramuscular and intrathecal administration was regarded as essential. The average duration of treatment for each

patient was 154 days. The average quantity of streptomycin necessary for the patient's recovery proved to be in inverse proportion to the patient's age. Seventy-two of the 113 patients with simple tuberculous meningitis and 15 of the 19 patients with tuberculous meningitis associated with miliary tuberculosis were discharged after recovery. Forty-one of the first group and four of the second group died. Seven deaths were partially due to the incidental occurrence of epidemic meningitis. Of the 87 patients discharged from the hospital as recovered, 20 had relapses, 17 in the group with simple tuberculous meningitis, and three in the mixed group. Three of the 17 patients had a second relapse, and one of the three had a third relapse. The most dangerous period for a relapse was the first trimester after recovery, and, with the third, the danger of relapse became minimal. Of the total 132 patients, 81 were alive one year after the last administration of the drug. Follow-up of the surviving children showed them to be in highly satisfactory condition without disability. Only one had an unsteady gait. Psychic disturbances or other forms of abnormalities were observed in only 2 per cent. One patient had diminished hearing.

Behr²¹ treated 26 patients with meningitis; eight survived. In three of the surviving subjects the diagnosis was not bacteriologically verified. Two out of 11 patients with miliary tb died. Only small doses of streptomycin were administered. The patients who survived were treated an average of six months. No details are reported. Intrathecal treatment is considered essential. Total daily doses of 5 to 15 g. of thiosemicarbazone did not have any appreciable effect.

Brainerd and Eagle²² studied the effect of streptomycin on 27 patients with tuberculous meningitis. Both intrathecal and intramuscular routes of administration were used. The daily dose intramuscularly varied from 12.9 to 130 mg. per kilogram of body weight, and the intrathecal dose from 0.4 to 9.3 mg. per kilogram. Toxic effects from the drug were frequent, although severe intoxication was uncommon. Nine patients died during the first four weeks of treatment without evidence of improvement; eight showed initial favorable response but later relapsed and died while still receiving treatment. Two patients showed initial favorable response but had slight persistent evidence of infection after completion of the five month therapeutic period; one patient was free of all evidence of central nervous system infection following the completion of five months' treatment, but meningitis recurred 100 days later; two were completely free of all evidence of meningeal infection at the completion of five months' treatment. These patients are completely well 16 and 17 months after the end of the therapeutic period. Five patients are still under observation. The average age of the improved patients was 8.7 years, with a range of 9 months to 42 years. The average age of the unimproved group was 31.2 years, with a range of

8 months to 58 years. Eleven of 13 females responded favorably, whereas only seven of 14 males were improved. There was no correlation between the therapeutic result and the number of cells in the cerebrospinal fluid or the concentration of cerebrospinal fluid glucose, chloride or protein. The duration of the disease before treatment had no effect on the outcome. Most patients responding favorably to treatment received more than 60 mg. per kilogram daily of streptomycin intramuscularly and over 2.0 mg. per kilogram daily intrathecally. Toxic reactions to streptomycin are common with high dosage but are a justifiable risk. The authors emphasize the importance of prolonged follow-up of treated patients and conclude that the prognosis of tuberculous meningitis is still grave.

Calnan et al.²³ report that of 54 patients with tuberculous meningitis treated with streptomycin between July 1947 and May 1948, 18 survived and were followed-up for two and a half to three and a half years. Two of the 18 original survivors died, reducing the survival rate to 30 per cent. Three patients relapsed but recovered after further treatment. Sequelae shown by the survivors were deafness in two, minimal hemiplegia in one, retarded development in one and intellectual defect in one. Audioraetric and vestibular tests done in 14 showed in all complete loss of vestibular response to caloric tests, yet none showed clinical ataxia. Pronounced hearing loss was present in two. Later manifestations of non-meningeal tuberculosis occurred in two recovered patients and responded to therapy. Slight variations in the spinal fluid of the survivors were observed but their significance could not be determined. The authors do not regard a patient as finally cured even two and a half years after streptomycin treatment. A further undetermined observation period is necessary.

Bunn²⁴ reports that in a two year follow-up on 100 patients with miliary and meningeal tuberculosis treated with streptomycin, 49 patients died and 2 of the 21 living patients are expected to die shortly. Seventy-six of these 81 patients died or are dying of their miliary and meningeal tuberculosis. Fatal relapses of one or the other were observed to occur as long as two years after an initial complete remission. Twenty-one patients survived at least 19 months after the end of treatment and a majority survived longer than 22 months. Since therapy averaged somewhat over four months, 18 of the 21 lived for over two years from the onset of their illness and the remaining 3 for at least 23 months. The treatment schedule of the 21 survivors was not obviously different from that of the patients who died. No patient of the 81 with meningitis survived who did not receive at least 45 separate intraspinal injections of streptomycin. It seems that this adjunctive route of administering streptomycin is advisable. About 20 per cent of the patients with meningitis alone survive. Less than 10 per cent of the patients with combined meningeal and miliary tuberculosis will survive.

Meningitis developed in approximately two-thirds of the patients with miliary tuberculosis. No series of cases can be safely evaluated for at least two years after the end of the treatment period. The success of therapeutic regimen is grossly overestimated if patients dying within two weeks after the start of treatment are excluded or if evaluation is made after only six months of observation.

Lassen and Neukirch²⁵ report that 11 of 32 patients with tuberculous meningitis and 2 of 12 with both tuberculous meningitis and miliary tuberculosis recovered with streptomycin therapy. Of 20 patients with tuberculous meningitis given only intramuscular streptomycin, 7 recovered; of 12 treated both intrathecally and intramuscularly, 4 recovered. The results of exclusively intramuscular treatment with streptomycin were thus as good as those of combined intrathecal and intramuscular treatment. The prognosis is very unfavorable in combined tuberculous meningitis and miliary tuberculosis. In the surviving patients, vestibular function was destroyed. The three adults but not the children were troubled by dizziness. BCG vaccination had not been done in any of the patients. No case of disseminated tuberculosis has been seen in persons in whom BCG vaccination was done. It is possible that BCG vaccination of all tuberculin negative persons would prevent the occurrence of tuberculous meningitis and miliary tuberculosis.

Complications in the Course of Treatment. In evaluating the sequelae and complications of the various forms of treatment of tuberculous meningitis, it is often difficult to determine the role of the agents used, the natural course of the disease, or both. Time alone will clarify the various factors involved. The following information is of some interest.

Shonenberg²⁶ observed deafness, blindness, spastic paralysis and other defects in patients who have survived tuberculous meningitis after streptomycin therapy. Such sequelae have usually been ascribed to incorrect dosage or inadequate purification of the antibiotic. In two children aged 9 and 6, adiposity of the type observed in Cushing's disease or in adiposogenital dystrophy developed during convalescence after tuberculous meningitis. In one child, adiposity was associated with striae distensae and osteoporosis. The other child had neither osteoporosis nor striae but a genuine adiposogenital dystrophy, and there were psycho-intellectual changes; intelligence was somewhat retarded, and silly behavior predominated. The so-called tuberculous meningitis is really, particularly when treated with streptomycin, a tuberculous encephalomeningitis. Either certain hypophyseal or diencephalic centers might have been involved in the disease process, or changes in blood perfusion and deficient function may have resulted from the vascular changes caused by tuberculous meningitis.

McKay et al.²⁷ report that among 90 patients treated for meningitis with repeated injections of intrathecal streptomycin, serious reactions occurred in 14 cases with 3 probable and 2 possible fatalities. The reactions consisted chiefly of shock-like states with slow irregular respirations, inability to handle adequately the secretions of the upper respiratory tract, convulsions, cerebellar signs and marked rises in body temperature with peak severity usually appearing five to six hours after intrathecal injection. The symptoms were not identical in each instance and occasionally occurred immediately after withdrawal of the lumbar puncture needle. There appeared to be some relationship between the size of the intrathecal dose and the occurrence of reaction. Milder reactions of pallor, irritability, loss of appetite and stupor occurred more frequently. Since equally good results can be obtained without it, discontinuance of the intrathecal use of streptomycin is advocated since it is uncomfortable to the patient, unnecessary and dangerous.

Howard et al.²⁸ state that hydrocephalus developed in more than 50 per cent of a group of children with tuberculous meningitis who were treated with streptomycin by both intrathecal and intramuscular routes. Hydrocephalus may develop either during the first month of the disease or later and is due to either excessive secretion of the spinal fluid or to lack of absorption because of the formation of exudates in the basilar cistern. The latter type has a poorer prognosis.

Bünger and Geiger²⁹ in 1948-1949 treated 106 patients with streptomycin. Some neurologic syndromes which may result are discussed. (1) Spinal meningitis is not due to irritation by streptomycin but to extension of the tb inflammation to the spinal meninges. Froin's syndrome is not typical of this and the Quckenstedt reaction may remain normal. Clinically, there is usually a paraspastic incomplete transverse lesion, the motor phenomena appearing first. (2) Optochiasmatic arachnoiditis is also regarded (tb meningitis now runs a protracted course owing to the use of streptomycin) as a syndrome of tb origin. In another case, hypophyseal signs—hypertrichosis and striae without obesity—were noted. Primary atrophy of the optic nerve was diagnosed in nine cases. (3) Hydrocephalus was found in practically all fatal cases. The opinion is expressed that the neurologic signs and death are probably a consequence of the cerebral edema. (4) Psychotic manifestations were often observed; these were probably connected with periods of increased intracranial pressure. Bünger³⁰ reports four cases of endocrine disturbances following treatment of tuberculous meningitis with streptomycin, para-amino-salicylic acid and amithiozone. One man of 42 developed obesity of the general dystrophic type, impotence and hemianopsia along with disturbances of carbohydrate metabolism. A boy 16 had dystrophia adiposogenitalis with striae and a

third nerve impairment. A woman aged 26 had marasmus due to diencephalic disturbances with cachexia, hypertrichosis and a left hemianopsia. A man 49 developed diabetes insipidus and disturbances of carbohydrate metabolism. Since similar cases developed prior to streptomycin therapy, these sequelae cannot be blamed on the treatment. The symptoms are probably due to vascular disturbances producing changes in the vegetative nuclei of the diencephalon.

Influenzal Meningitis

Next to tuberculous meningitis, the advances in the treatment of influenzal meningitis are probably the most gratifying.

Appelbaum and Nelson³¹ made a study of 90 cases; there were 28 cases under one year, 43 between one and three, 15 between four and ten, and one each at the years 13, 29, 44 and 51. A great variation in time before treatment is represented by these cases, varying from one day to five weeks. All but two had *H. influenzae* type B, one had type F and one was unclassified. Sensitivity tests to streptomycin were made in 50 cases. 26 of the patients had blood cultures and of these 18 were positive for *H. influenzae*. Seventy-three of the cases had dihydrostreptomycin intramuscularly and intrathecally. Seventeen cases were treated without the intrathecal administration of the drug. These latter 17 made a complete recovery. The ages of the three fatal cases were 11, 12 and 17 months. One of these was a fulminant toxic case and the patient died with pulmonary edema 48 hours after the onset of illness. There were 19 cases with sequelae. Four of these had total or partial deafness. One had hydrocephalus and defective vision. One other had hydrocephalus alone. There were two with blindness and mental impairment, and one case had slight hemiparesis. In addition to dihydrostreptomycin, all but one of the cases were also treated with sulfadiazine. Anti-influenza rabbit serum was used in 17 instances. The use of intrathecal therapy is discussed.

McMorrow and Top³² treated 38 males and 29 females with *H. influenzae* type B. meningitis during a five-year period. Thirty-three of the patients were under two years of age and 11 of the 17 fatalities (65 per cent) were in this age group. The corrected death rate for patients under two years was 18.2 per cent. Thirty-seven patients were treated with sulfadiazine and serum, five with sulfadiazine and streptomycin, 18 with sulfadiazine, serum, and streptomycin and four with sulfadiazine alone. Two did not receive specific treatment; four patients admitted and treated at the end of the third week of illness died. The prognosis is likely to be unfavorable in the age group under two years if treatment is delayed beyond the 14th day. The fatality rate was the same for patients who received sulfadiazine and serum as for those who received streptomycin in addition.

Serum therapy was ineffective in the group under two years of age if administration was delayed beyond the 14th day.

Chloramphenicol had proved of value in the treatment of influenzal meningitis. Prather and Smith³³ report the recovery of 15 consecutive cases of *H. influenzae* meningitis of average severity. Eight of these were under one year of age. They were all proved bacteriologically to be *H. influenzae* type B. Chloramphenicol was used orally or introduced by gavage. In general, the dosage was 50 to 100 mg. per kg. as a first dose and then 250 mg. every eight hours. There were no toxic symptoms from the drug. In every case the spinal fluid was sterile on the second puncture. The authors believe that it is the drug of choice in *H. influenzae* meningitis.

McCrumb Jr., Hall et al.³⁴ successfully treated 12 children with *H. influenzae* meningitis with chloramphenicol. It was their impression that the clinical response to treatment was striking. There were no fatalities.

Swift and Bushby³⁵ state that a satisfactory response was obtained in eight patients with *H. influenzae* meningitis treated intrathecally and intramuscularly with polymixin. Seven patients recovered completely and one died. The spinal fluid became sterile within 24 to 96 hours. The sugar content of the spinal fluid and the leucocytosis were reduced in from 24 to 48 hours. Pyrexia diminished in from one to eight days. No relapse occurred. High concentrations of polymixin were maintained in the spinal fluid by administration of two injections per day, although moderate concentrations can be obtained for 24 hours with a single dose of 40,000 units. Once the spinal fluid was sterile, single daily doses were adequate. The optimum duration of intrathecal treatment has not been determined.

Pneumococcic Meningitis

Simpson and Holley³⁶ report that of 40 patients with pneumococcal meningitis, 62 per cent were over 15 years of age. All but three received sulfonamide, and intramuscular penicillin was administered to all but nine. Twenty-five received intrathecal penicillin. The recovery rate was 60 per cent for the entire group, 36 per cent for patients over 50 years of age, 62 per cent in patients under two years. The recovery rate in patients receiving intrathecal penicillin was 60 per cent. There were no toxic reactions to intrathecal medication. Relapse occurred in three patients after seven to nine days of sulfonamide therapy, suggesting that the sulfonamides should be continued for at least a week after the spinal fluid becomes sterile.

Nemir and Israel³⁷ state that of 15 patients from 4 weeks to 11 years of age with pneumococcic meningitis, 14 recovered. In a 10-month-old infant admitted on the fifth day of illness, severe hydrocephalus developed and he died nine months later. A follow-up study on 11 patients made from

six months to five years after the infection showed no residuals attributable to the meningitis. One patient recovered without the use of intrathecal medication, and a second had only negligible amounts intrathecally. Three others had only one intrathecal injection. One infant four weeks of age recovered. All patients received penicillin intramuscularly in fairly large amounts and sulfonamides orally. Two patients were given penicillin intravenously also.

Other Types of Meningitis

Hoyne and Herzon³⁸ reported 34 recoveries and 29 deaths following streptococcus viridans meningitis. The incidence of this type of meningitis was found to be from 0.3 per cent to 2.4 per cent of cases of purulent meningitis. The disease followed subacute bacterial endocarditis in only 13 per cent of the cases, and ear, nose and throat infection in 33 per cent. No source was found in 35 per cent. Therapy in streptococcus viridans meningitis is determined by the sensitivity of the organism to all the sulfonamides and antibiotics. When sensitivity tests are not available, a combination of penicillin and sulfonamide is the treatment of choice. At least 50,000 units must be given every three hours intramuscularly and two to three grains per pound of body weight per day of a sulfonamide.

Teng³⁹ treated 13 patients with various types of purulent meningitis with bacitracin. Previously the cases had been resistant to penicillin, other antibiotics and sulfonamides. Of eight patients treated after other antibiotics had failed, six survived. Of five patients treated primarily with bacitracin, three recovered. The cases which died were complicated by other conditions such as tumor in the pineal region, thrombosis of the middle cerebral arteries, multiple brain abscesses, a long-standing extensive purulent encephalitis and an undisclosed brain abscess.

Myerson⁴⁰ reports a case of meningitis occurring during gold therapy for rheumatoid arthritis. The meningeal symptoms developed within less than three weeks of the onset of gold therapy. The patient was given BAL 150 mg. intramuscularly every four hours for 4 doses, and 1.5 cc. daily thereafter for six days with prompt subsidence of meningeal signs. Because of the temporal relation between the administration of gold and the development of symptoms, the prompt response to BAL and the inability to prove another etiologic agent, gold was considered as the responsible factor.

Poliomyelitis

Little of fundamental importance has been added to our knowledge of poliomyelitis during the past year. The main contributions on this subject include the investigations of the mode of transmission of the virus, further

evaluation of the role of tonsillectomies and the various prophylactic injections as precipitating causes, the role of the sympathetic nervous system in the symptomatology and the evaluation of various palliative forms of treatment.

Greenberg et al.⁴¹ report on an outbreak of poliomyelitis occurring in New York City in 1949 with a total of 2,446 cases and 179 deaths. About 75 per cent of the cases were in children less than 15 years of age and 58 per cent of the cases were in males. A spinal type of paralysis was shown in 1,109 cases (45.3 per cent) and a bulbar or bulbospinal type in 393 (16.1 per cent). The secondary attack rate in homes where a case had occurred was 15 times the attack rate for the city as a whole. The ratio of cases in school children to total cases did not increase after the opening of the school. Recent tonsillectomy appears to predispose to the development of poliomyelitis, especially the bulbar type. Exercise during the onset of poliomyelitis adversely affects its course.

Margreaves⁴² reports on 110 cases of poliomyelitis occurring in Cornwall in 1949, an incidence of 0.3 per 1,000 of population. Individual cases of interest are those of two expectant mothers who developed poliomyelitis at or about the date of their confinement. In one, severe paralysis developed four days before delivery, labor was normal and the baby unaffected. In the other, paralysis was first noted 28 days after confinement. The baby, who was breast fed, had symptoms suggestive of pre-paralytic poliomyelitis three weeks after birth, followed four days later by convulsions. At present, the infant has a slight weakness of the muscles of the left shoulder girdle. The high age of the patients in this epidemic, their sporadic distribution, the lack of history of contact between cases, together with the sudden cessation of the outbreak after superchlorination of the water supply, known to be contaminated, suggest water dissemination of the virus.

Mackenzie⁴³ states that during recent years it has been shown that poliomyelitis virus is discharged in the feces of infected individuals, and that it is capable of surviving and retaining its virulence in sewage and in water for long periods (up to 188 days). Consequently, considerable attention has been given to the possibility that poliomyelitis may be spread in a manner similar to that of the excremental diseases. The evidence for carriage of the poliomyelitis virus by water and the means available for preventing this are considered. While the possibility of transmission of the poliomyelitis virus by water must be accepted, there is no evidence that it has ever been distributed in a public water supply in sufficient quantity to cause infection, or that it is capable of surviving in such quantity, if at all, the purification processes which have in the past been applied to the London Metropolitan Water Board's water.

MacLean⁴⁴ states that the New Zealand poliomyelitis epidemic of 1947-

1949 differed in some respects from epidemics of other infectious diseases commonly believed to be spread by droplet infection: (1) There were a number of isolated cases in remote areas without any obvious source of infection. (2) Poliomyelitis occurring in a school child was infrequently followed by a second case at the same school. (3) The spread of the epidemic from one part of the country to another was slow. (4) There were abortive outbreaks. A plausible explanation of these features is that fecal contamination of the hands may cause the virus to be spread to inanimate objects, and thence to the hands of other people, who may in turn become carriers. No direct evidence that this was in fact the mode of spread is presented, and alternative explanations are not considered. It is suggested that the capacity of the poliomyelitis virus to survive outside the human body may be a recently acquired characteristic and that this may explain why poliomyelitis has changed from an endemic to an epidemic disease. The only control measure likely to influence the spread of the disease is strict personal hygiene and hand washing after defecation and before taking or handling food.

Behrend and Hansen⁴⁵ report on approximately 450 cases which were registered in the 1947 poliomyelitis epidemic at Hamburg. At the beginning of the epidemic, isolated cases were observed in various parts of the city and suburbs, apparently without connection. Then, groups of several cases appeared round the isolated ones; these groups enlarged and joined one another. The clinical course was different from one area to another, but it is not suggested that these differences be imputed to different strains of virus. Along with the 1947 epidemic in England, a poliomyelitis epidemic occurred in the district of Luneburg, the peak of which coincided with the beginning of the Hamburg epidemic. In Hamburg, cases increased suddenly at the end of July, and for four months there was a uniform rise of the incidence curve, whereas the decline of the epidemic showed an irregular course over three months. The female/male incidence ratio, at first 1:4, changed gradually and towards the end of the epidemic was 1:082. The incidence in different age groups are also changed, the attack rate being highest in the children of one to four years during the initial phase of the epidemic, and in later stages in older groups.

Lenarsky et al.⁴⁶ reviewed 526 cases of poliomyelitis observed at the Willard Parker Hospital in New York. These cases represent a concentration of seriously involved patients. Thirty-nine of the 40 deaths in this group were due to bulbar involvement. Complete vascular collapse resulting from failure of the vasomotor center accounted for 33 deaths. The use of the respirator and of central stimulation minimized fatalities from respiratory difficulties due to peripheral or central failure. Administration of an antihistaminic drug in 10 patients seemed to have no therapeutic effect.

Aureomycin was of no value. The use of drugs for vital center stimulation was effective in some instances of bulbar involvement. The latter was not considered a contraindication to the use of the respirator.

McLeod⁴⁷ states that during an epidemic of 98 cases of poliomyelitis in Belfast, an attempt was made to correlate the site of paralysis with previous inoculations of diphtheria toxoid. All but ten of the children showed paralysis. In one patient immunized in the right hip, paralysis of the right leg developed after eight days. Another patient who was immunized in the left arm developed facial paralysis 23 days later. In three patients in whom poliomyelitis occurred within one to three months after injection, the paralysis did not involve the arm in which the inoculation was given. In 28 children in whom paralysis developed more than three months after inoculation the paralysis affected the leg more frequently than the arms where the injection had been given. An association between the site of inoculation and the site of paralysis was not observed after 6,250 inoculations of purified diphtheria toxoid in children less than nine years. While this limited experience does not prove that the site of inoculation and the site of paralysis in poliomyelitis are related, the author's experience suggests that purified diphtheria toxoid is a relatively innocuous antigen as far as induction of poliomyelitis in the inoculated limb is concerned.

Goerke⁴⁸ does not consider statistically significant the slightly higher incidence of paralysis among children recently vaccinated or immunized over that in children who were not. He concludes: "It appears inadvisable to permit the possible chance occurrence of poliomyelitis following injections to interfere with the continued mass elimination of diseases equally crippling and fatal." The incidence of paralysis for the year 1948 among the 27 children with poliomyelitis under 12 years of age who were immunized or vaccinated was 77.8 per cent, and among the 843 cases of poliomyelitis for the year in this age group it was 74.3 per cent. Among the total of 1,321 cases in 1948, there were 30 cases with onset within 34 days after an injection of some kind (including 18 cases with onset within 10 days). In eight patients, paralysis was related to the site of injection; in eight it was not; in eight, site of injection could not be identified; in six, there was no paralysis.

McCloskey⁴⁹ investigated 620 cases of poliomyelitis in regard to a possible relation of prophylactic inoculations to the onset of poliomyelitis. In 53 patients who had received an injection of diphtheria toxoid or pertussis vaccine alone or in combination, within three months of the onset of symptoms, exact information on the date and site of the injection could be obtained. The severity of paralysis in the last inoculated extremities of children who had received pertussis vaccine alone or in combination was greater than in those of children who had received diphtheria toxoid alone

and also greater than in the corresponding extremities of uninoculated children. There is thus evidence that recent inoculations of pertussis vaccine alone or in combination with diphtheria toxoid are more likely to be followed by paralysis than recent inoculation of diphtheria toxoid alone and that the paralysis following inoculations with pertussis vaccine alone or in combination is more severe than that following inoculations with diphtheria toxoid alone.

Anderson and Skaar⁵⁰ analyzed the case histories of 2,709 persons who had poliomyelitis during the 1946 epidemic in Minnesota in reference to injections or immunizations. It was impossible to determine precisely whether the attack rate was higher among recently immunized persons. However, there was a high degree of correlation between the site of paralysis and the site of injection. The paralysis was more severe in children recently immunized. There is no evidence that the antigen influences or in any way conditions the response to poliomyelitis for longer than one month. Since immunization is an elective procedure it can well be delayed during outbreaks of poliomyelitis, but there is no suggestion that the postponement should be more than temporary.

Sedallian and Gaillard⁵¹ state that in about 5 per cent of cases of poliomyelitis, paralysis may develop in two stages, i.e., new peripheral paralysis may develop within eight days to one month after the first appearance of paralysis and may be localized in parts of the body not previously involved. Five cases of this type were recently observed. In an illustrative case, a patient with flaccid quadraplegia and meningeal irritation, a month after the acute phenomena had disappeared, experienced an attack of bulbo-respiratory involvement with tracheo-bronchoplegia and paralysis of the intercostal muscles and diaphragm. Although all of the patients were treated with convalescent serum, folic acid and roentgen irradiation of the cord, this therapy did not prevent the development of the second stage of paralysis. In most of the patients of this type the upper levels of the cord were involved. Seventy-five per cent of the patients had severe quadraplegia or respiratory paralysis or both. Intercurrent infection, such as chicken pox and infectious pulmonary complications, seem to predispose to this type of paralysis. The pathogenesis remains doubtful. Although the possibility of a relapse or a second attack may be considered, it is possible that the virus is capable of persisting in the nervous system of certain patients or of reinfecting the organism by the endogenous route. Weakened resistance due to intercurrent infection and prolonged presence of the virus in the feces may play some part.

Lans, Stein et al.⁵² studied six patients with bulbar poliomyelitis who were found to have a potassium deficiency. Treatment with intravenous potassium chloride resulted in a marked improvement in respect to in-

creased energy and diminished lethargy and listlessness. Patients with bulbar poliomyelitis who are unable to eat will develop a potassium deficiency unless adequate potassium intake is provided. Severe prolonged potassium deficiency can be lethal and in patients with bulbar poliomyelitis may be a factor in the high mortality rate. Adequate control of the electrolyte balance is important and must include potassium therapy.

Cook, Hartmann et al.⁵³ state that gastrointestinal complications of bulbar poliomyelitis appear to be more common than previously realized. Of five children reported between the ages of 3 and 11 with severe bulbar poliomyelitis complicated by gastrointestinal perforation and/or hemorrhage, four died. The gastrointestinal lesions were associated with respiratory center involvement in all. A relationship between midbrain damage and the gastrointestinal lesions is postulated. Routine guaiac tests should be performed on the stools of all patients with acute bulbar poliomyelitis. Therapy should include blood transfusions.

Neuman⁵⁴ draws attention to patients with poliomyelitis who complain of pain of a decidedly radicular type. Exact localization was impossible, pressure points could not be detected and the entire extremity was involved. In contradistinction to the continuous pain in patients with poliomyelitis, this pain was characterized by severe nocturnal exacerbations. It is assumed that inflammatory changes in the posterior roots were the cause of this pain. This assumption was corroborated by the great increase in the protein content in the spinal fluid. The radicular pain always appeared in segments corresponding to those of paralysis. It is assumed that in the radicular form of poliomyelitis, the virus has a special affinity for the posterior nerve roots and that these are more severely involved in the mesodermal reaction in the form of a radiculitis.

Albrecht and Locke⁵⁵ studied 200 patients concerning their physical activity from three days before to a number of days after the onset of poliomyelitis, and the degree of residual paralysis present five and one-half to seven months after onset. Deaths and severe paralysis in children are not related to the degree of physical activity either shortly before the onset or at any time during the illness, but in adults they may be attributed in part to the amount of physical activity in the meningeal stage. Age is a major factor in the prognosis of poliomyelitis. Adults, irrespective of activity, are more severely affected than children. Other factors also affect the prognosis.

Brahdy and Katz⁵⁶ recorded fatality rates for a group of patients with poliomyelitis who were transported to the hospital over long distances and for a comparable group who were transported short distances. The results indicate that transportation over a long distance may be harmful to a patient in the acute stage of poliomyelitis.

Zellweger and Morf⁵⁷ state that trophic disturbances in the late stage of poliomyelitis may involve the skin, muscles and bones. The skin may be cold and damp and show a reddish blue discoloration associated with thinness, glossiness and desquamation. The musculature atrophies, as revealed by a decrease in circumference. This atrophy is a result not only of the trophic disturbances, but also of inactivity. Trophic disturbances in the bones are manifested by osteoporosis, which is more severe than that resulting from inactivity. Whereas impairment of motor function is often improved or remains stationary after the acute inflammatory stage of poliomyelitis, the trophic disturbances have a tendency to increase with time, and trophic ulcers may result. The trophic disturbances are attributable to changes in the vasomotor nervous system. Capillaroscopy, skin temperature readings and oscillometric measurements provide objective evidence of these trophic disturbances. During the initial phase, skin temperature and oscillometric response are increased on the affected side, but during the paretic stage both these measurements are decreased in comparison with the unaffected side. Treatment aimed at overcoming these vasomotor changes should become an essential part of poliomyelitis therapy. The authors describe the results obtained with physiotherapy and sympathectomy.

Coffee and Paul⁵⁸ report that to the 49 previously recorded cases of second attacks of acute anterior poliomyelitis, another case in which there were two distinct attacks, separated by a 24 year interval, is added. Second, attacks of paralytic poliomyelitis in the same individual, although rare, do occur. New symptoms occurring two or more years after the initial episode should be considered a reinfection, while the occurrence of additional symptoms or extension of previously existing motor impairment during the few months immediately succeeding an initial should be considered a recrudescence of existing infection. The second attack may be due to infection by a strain of virus antigenically unrelated to the one producing the initial infection, failure of antibody production or loss of immunity with the passage of time.

Hoyne and Lipton⁵⁹ present a second attack of poliomyelitis with fatal termination and autopsy findings. It has been suggested that second attacks of poliomyelitis are due to an immunologically different strain against which the patient has no previous immunity.

Sarnoff et al.⁶⁰ report that in nine patients with central respiratory irregularities due to bulbar poliomyelitis, the irregularities could be suppressed in each case by electrophrenic respiration and regular effective ventilation provided instead. Unlike the tank respirator, the electrophrenic respirator is not a hazard in the presence of circulatory inadequacy and may actually elevate the blood pressure and cardiac output in these cir-

cumstances. While the usefulness of the electrophrenic respirator cannot be considered as established in bulbar poliomyelitis until additional experience has been obtained, the foregoing data are encouraging. The apparatus should not be used unless the operator has acquired sufficient proficiency in its use. It is obvious that one phrenic nerve must be wholly or partially uninvolved by disease if effective electrophrenic respiration is to be performed. The electrophrenic respirator consistently and strikingly diminished the restlessness and hypertension in one patient and achieved similar results in others. The mechanisms involved are not known. It was thought that nursing care was facilitated in the treated group of patients in comparison to what is usually the case with tank enclosed patients.

Smith, Graubard, et al.⁶¹ have been impressed by the regular occurrence of lesions in the sympathetic ganglions of patients who died of poliomyelitis and think that these give a rational anatomic explanation for vasomotor disturbances, ischemic pain and other evidence of sympathetic inability so common in the acute phase of the disease. With this rationale as a basis, they have attempted to control the symptom complex of pain in poliomyelitis by the use of sympatholytic drugs such as priscoline. Six hundred and sixty three patients were treated with priscoline hydrochloride. In the dosage used morbidity was minimal. The patients began to improve within 30 minutes after oral administration of the drug. When the dosage was sufficient to produce a therapeutic effect, the pain either diminished or disappeared completely. In most cases, muscle tightness diminished and the patients were able to move the nonparalyzed parts more freely. Appetite and sleep improved, muscle twitchings receded. Cold clammy skins became warm and excessive sweating disappeared. Nearly all patients manifested some form of progress and their clinical status improved so rapidly that it was possible to transfer the majority of them relaxed and free of pain to their homes or orthopedic hospitals in 7 to 14 days. Further investigation of the use of sympatholytic drugs in acute poliomyelitis is indicated.

Geisler, Mustard and Anglin⁶² state that pain and muscular tenderness are not of great importance in the absence of paralysis. When paralysis is present, every effort should be made to prevent the development of painful contractions leading to deformities. Twenty-five cases observed at the Children's Hospital in Toronto are quoted in support of this opinion. Priscoline was found of little value and is not recommended for routine clinical use.

Appelbaum and Saigh⁶³ treated 38 patients with non-paralytic poliomyelitis with aureomycin. The use of aureomycin early in the disease did not appear to affect favorably the clinical course of poliomyelitis.

Fox and Hornberger, Jr.⁶⁴ report on 29 patients with bulbar and spino-bulbar forms of poliomyelitis who received phenosulfazole. The mortality

rate was 34.5 per cent. During the same period, 19 patients who did not receive the drug showed a mortality rate of 42.1 per cent. The difference was not statistically significant. There was no alteration in the length of temperature elevation or the length of hospitalization in the group receiving the drug and instances of drug toxicity were not noted. It is the author's impression that phenosulfazole offered little in the treatment of poliomyelitis.

Binet et al.⁶⁵ treated five patients with poliomyelitis with an adrenal gland extract (cortin), 1 cc., of which corresponded to 125 gm. of the fresh gland. The daily dose was 2 cc. given in two divided doses intramuscularly. The duration of the treatment varied according to the patient. Treatment was practiced systematically in patients who had a fever on admission. There was a rapid drop in temperature by lysis. Apyrexia or a subfebrile state resulted within three to five days in all patients. The paralysis did not progress in any of the patients; it seemed improved in two patients on the third or fifth day of the treatment. There was a pronounced improvement in the general condition of the patients between the fourth and sixth days after the institution of treatment. It is too early to draw definite conclusions but the treatment with cortin proved innocuous.

Steegman and Davis⁶⁶ report on a ten-year-old girl with acute spinal and bulbar poliomyelitis who suffered respiratory difficulty. After a period of anoxia, evidence of cerebral injury developed characterized by stupor, interspersed with delirium and hysterical-like behavior, labile emotionality, convulsions, clonic muscular twitchings, blindness, and disturbed function of the gastrointestinal tract. Hypertension and heart block complicated the picture. Death occurred in about three months.

Encephalitis

The literature on encephalitis is concerned with the intracranial complications of systemic diseases, especially those following or complicating the exanthemata, those following bacteremia and virus infections, brucellosis and other conditions that are often difficult to diagnose. Most of these have been reviewed in previous volumes of this publication.

Anderson and Morris⁶⁷ report on a boy (one of uniovular twins) previously healthy who developed a generalized convulsion at the age of two years and four months, and was left with a transient right hemiplegia for five hours. His illness was diagnosed as mumps encephalitis. Three months later he and his twin were immunized with combined diphtheria and pertussis antigens. His twin remained well but the patient had a generalized convulsion 36 hours later. Studies done eight months later showed dilatation of the left lateral ventricle and diminished electrical activity of the left cerebral hemisphere. A year later there was some recovery but the patient still

had a limited vocabulary and was mentally retarded. The pathogenesis is unknown but in view of the serious neurologic sequelae it is suggested that pertussis vaccination should not be done if there is a history of convulsions in the child or the family.

Bernstein and Wolff⁶⁸ state that the nervous system appears to be affected in less than 1 per cent of patients with infectious mononucleosis. Since many parts of the nervous system may be involved, the symptomatology is variable. Serous meningitis, meningitis, encephalitis, meningoencephalitis, polyneuritis and peripheral neuropathy have been described. It appears that the nervous system is directly invaded by the causative agent. The spinal fluid may show an increase in lymphocytes and/or protein. Commonly the spinal fluid may show changes without any concomitant clinical involvement. The prognosis is excellent, 85 per cent of patients show a complete recovery. Males are more commonly affected than females. Since systemic signs of infectious mononucleosis may be minimal and the clinical neurologic picture is indistinguishable from that caused by many other agents, heterophil antibody tests are advised on all patients with idiopathic diseases of the nervous system.

Mulder⁶⁹ reports on a serious epidemic of western equine encephalitis which occurred in Colorado in the summer of 1949 but was not recognized until late because many of the patients were thought to have an atypical form of poliomyelitis. Twenty-five cases were observed. The epidemic occurred in late August and early September. The patients presented, in general, two clinical syndromes. Young children from one to six months of age suffered a brief acute illness while in the adults, mainly males, the symptoms were severe and prolonged. The infantile form was found in four children, all under 12 weeks of age. All had high fever and continuous convulsions which began abruptly and did not respond to the usual therapy. These manifestations persisted three to seven days and then abruptly disappeared. The deep reflexes were more active in the extremity from which the convulsive movements spread. Cog wheel rigidity and signs of meningeal irritation were present. The adults showed considerable variation in the severity of clinical symptoms: usually the illness began with fever, chills and malaise and were soon followed by severe headache and drowsiness or coma. Some patients showed delirium. Less severe symptoms included pain in the back, nausea and vomiting. Nuchal rigidity was found in all cases. Tremor, dysarthria and upper motor neuron symptoms occurred in the more severely ill. In some cases, central autonomic functions were disturbed and the patients showed a hypothermia. Respiratory arrest occurred in two. Spinal fluid examination during the first few days revealed a mild increase in pressure, a pleocytosis of from 25 to 600 cells, chiefly polymorphs, and increased sugar and protein. During the second week the

cells in the spinal fluid showed a predominance of lymphocytes. The blood showed a mild leukocytosis. Death occurred in 12 per cent of the cases, usually in the first 48 to 96 hours. Convalescence was prolonged in the adults and recovery usually took three to four months. In the infants, recovery was complete in a few weeks. Sequelae were frequent. In infants there was an inability to use one side of the body as well as the other. One child continued to have focal convulsions. In adults the sequelae were manifested by rigidity, dysarthria, facial masking, weight loss and organic mental disturbances. Treatment was symptomatic.

Mulder, Parrott and Thales⁷⁰ followed 15 patients with western equine encephalitis for six to eight months. All three infants have an inability to use one side of the body as well as the other and one has focal convulsions. The severity of sequelae in the 12 adults seems to be directly related to the duration of coma in the acute illness. Nine of the 12 have sequelae. Six have a clinical syndrome similar to parkinsonism. In three, the sequelae were minimal and in three moderate. Some showed organic impairment of psychologic functioning.

Hullinghorst, Burns et al.⁷¹ report that during the summer of 1949 an epidemic of Japanese B. encephalitis occurred in Korea. In 5,548 cases there were 2,429 deaths. Sixty-three per cent of the cases occurred in individuals from 3 to 13 but the age span ranged from 1 to 60 years of age. In two-thirds of the cases, the onset was acute. The most frequent symptom was fever of 39 to 40° C., headache, anorexia, nuchal rigidity, nausea and somnolence. The most prominent sign was a cloudy sensorium. Other prominent abnormalities included carpopedal spasm, partial or complete paralysis of the extremities, bowel or bladder incontinence, strabismus, ptosis, facial palsy and hemiplegia. A neurotropic virus was recovered from the brain in a fatal case. This agent and two others that were observed elsewhere were identified as that of Japanese B. encephalitis. Serologic studies also supported the etiology.

Orbison, Reeves, et al.⁷² reviewed 83 cases of amebic brain abscess found in the literature and five additional cases are reported. In 7 of the 88 cases, the abscess was found in the cerebellum. In six cases the amebic abscess was isolated in the brain without associated involvement of the liver or lung. The initial lesion is most likely in the cerebral substance itself rather than in the leptomeninges. The fundamental pathologic feature was a characteristic predominant central necrosis surrounded by mononuclear cell infiltration without reparative gliosis. Amebic brain abscesses occur in 3 to 4 per cent of cases following liver or lung abscesses. There are no specific clinical manifestations characteristic of the infection. In about half the cases the onset of neurologic symptoms was abrupt and in such cases the course was usually fulminating. Survival was usually longer in cases with

an insidious onset. The most common clinical manifestations included headaches, convulsions and alteration in the mental state, particularly in respect to dulling of consciousness. Focal symptoms are relatively few but visual disturbances are fairly common. Cerebellar symptoms may occur. In the majority of cases, the temperature is elevated to between 101° and 103°. Meningeal signs are frequently found. There are no characteristic spinal fluid findings but abnormalities are frequently found. The prognosis is poor; only one patient survived. As to therapy, intensive antiamebic drug administration along with conservative surgical procedures to obtain decompression are recommended. If the patient survives and encapsulation occurs, further surgery would be indicated.

Brown and Peyton⁷³ report that in three cases of brain tumor (dermoid cyst, glioblastoma multiforme and cerebral varix involving the third ventricle) symptoms of meningeal irritation were the presenting complaint. The meningeal reaction may result from the irritative effect of necrotic tumor cells or myelin destruction in the perineoplastic area. Intracranial neoplasm should be accorded an important place in the etiology of meningitis and any case of meningitis with an abnormal course should be viewed with suspicion and studied further to determine the etiology.

Bolus and Wilkinson⁷⁴ reported that four cases of herpes zoster received aureomycin in doses of 250 mg. three or four times a day along with low voltage roentgen therapy. Good results were obtained in all cases. A fifth patient who received chloromycetin also showed good results.

VASCULAR DISEASES

Except for the advances made in the recognition and treatment of intracranial aneurysms, little startling has been reported in the management of patients with cerebral vascular disease.

Webster, Dolgozf and Guidjian⁷⁵ present three cases of spontaneous thrombosis of the common, external and internal carotid arteries and one case of thrombosis of the internal carotid artery. This syndrome may occur at any age of life, males are more frequently affected than females, and the left side of the neck is involved approximately five to six times as frequently at the right. The symptoms are essentially those of a cerebrovascular accident but in a significant number of cases of thrombosis of the carotid artery other features have appeared with a sufficient degree of regularity to make them worthy of note. Headache is a frequent premonitory symptom. Transient and recurrent prodromal signs, suggesting psychosomatic complaints were common. The onset may be explosive simulating the usual cerebrovascular accident or slowly progressive with neurologic symptoms of varying severity. The syndrome may be associated with homolateral blindness and optic nerve atrophy. In some cases there are no

disabling symptoms or signs. The diagnosis may be by palpation of the neck and of the temporal arteries. Arteriosclerosis was the important etiologic factor.

Fisher⁷⁶ presents eight cases of occlusion of the internal carotid artery. This condition is much commoner than has heretofore been believed. The carotid sinus is the region of predilection, and the basic pathologic process is atherosclerosis. The clinical picture, although variable, is highly characteristic. The basic feature is severe hemiplegia preceded by premonitory paralysis, paresthesia, blindness, dizziness and aphasia or unconsciousness. Headache is very common. There are often fleeting neurologic symptoms. The exact diagnosis of occlusion of the internal carotid artery rests on arteriography or pathologic study, but the clinical features serve to distinguish it in most cases. Hemiplegia of unknown cause in younger patients is often due to this condition. The absence of carotid pulsation in the neck during the acute phase of hemiplegia may be diagnostic. Postoperative hemiplegia, as well as stroke following vascular collapse, is often due to thrombosis of the internal carotid artery distal to the extreme atherosclerotic narrowing in the region of the carotid sinus, and cerebral embolism may arise from thrombotic material lying in the carotid sinus.

Conley and Rand⁷⁷ tabulated from the literature 20 cases of spontaneous subarachnoid hemorrhage occurring in noneclamptic pregnancy and reported eight new cases. In only four, did the subarachnoid hemorrhage occur during labor. In 14 it occurred prepartum and in 10, post-partum; in 6 of the latter within 24 hours after delivery. The maternal mortality rate was 42.9 per cent, the fetal mortality rate 26.3 per cent. All such cases should have the benefit of cerebral arteriography and if the condition of the patient permits, accessible vascular lesions discovered should be surgically explored. Caesarean section is probably the best mode of delivery. Termination of pregnancy may be justified as well as prevention of future pregnancies.

Biemond⁷⁸ described four cases of total occlusion of the basilar artery. One was due to a syphilitic endarteritis, two were caused by an arteriosclerotic thrombus, and in the fourth, the artery had been compressed during an operation. There is no clearly delimited complex of symptoms in basilar thrombosis as the distribution of the softening varies from case to case. Among the changing symptoms are included paralysis of conjugate eye movements, pupillary changes, slight sensory changes in the trigeminal area and on the body, fleeting blindness, hemianopsia, drowsiness or coma. The major syndrome always remains that of tetraplegia with dysarthria and dysphagia. The onset is acute although usually with a prodromal period. After the acute beginning a remission may occur during which it may be found that transitory hemiplegia may change from one side of the body to

the other. If it is possible to make a diagnosis before complete tetraplegia and pseudobular paralysis have developed there is a chance to initiate therapy which may possibly forestall a definite occlusion.

Steegman⁷⁹ reports 17 cases of pontile hemorrhage. The condition occurred more frequently between the ages of 40 to 60 and about equally in the two sexes. The etiology in 15 cases was hypertensive arteriosclerotic cardiovascular disease. This was complicated by diabetes in one case, and by syphilis in two. Toxemia of pregnancy was present in two cases. The lesion in most cases was a large relatively compact hemorrhage which had a tendency to rupture into the fourth ventricle. The onset in the majority of cases was accompanied by sudden collapse and unconsciousness. Premonitory symptoms were sometimes absent but when present consisted of headaches, dizziness, vomiting, paresthesias or numbness with or without weakness of one or more extremities. There was no uniform clinical picture. In some cases, weakness of the ocular, facial or bulbar muscles was evident. This was sometimes accompanied by paralysis of the extremities or by muscular rigidity and trembling. Spinal shock with flaccid extremities was as frequent as rigidity. Contracted or pin point pupils were present in 65 per cent, bloody spinal fluid in 75 per cent and terminal hyperpyrexia in 25 per cent. Disturbed autonomic function characterized by exophthalmos, sweating or flushing was observed in a few cases. Fourteen patients died within ten hours. Some disturbance in respiratory rate and rhythm occurred in every patient. Thirty per cent showed respiratory failure and 35 exhibited slow labored gasping or apneustic respiration. In one case the respiratory failure was associated with multiple discrete lesions at the mid pontile level. These lesions were bilateral, paramedian and involved the inferior portion of the reticular substance of the tegmentum, and the upper portion of the bulbar region.

Epstein⁸⁰ reports that of 74 cases of primary massive intracerebral hemorrhage, seven were located in the pons. Primary massive pontine hemorrhage is a terminal event occurring in patients with severe hypertensive cardiovascular disease. Clinically, it is characterized by sudden onset, deep coma, bilateral neurologic signs and a rapidly fatal course. The pupils are frequently miotic. Hyperpyrexia may be present and usually occurs terminally. Convulsions may occur but are not attributable to involvement of specific pontine areas. The spinal fluid may be grossly or microscopically bloody; its pressure is usually elevated. Encephalomalacia of the pons may usually be differentiated by the absence of severe hypertensive cardiovascular disease, by a longer duration which permits the development of specific pontine signs and by the absence of blood in the spinal fluid.

Moersch and Sayre⁸¹ report on 26 cases of dissecting aneurysm of the aorta in which 12 patients (46 per cent) had some neurologic complications.

Eighteen of the cases were men. The age range was 30 to 72 years with the average age of onset between 51 and 56 years. The most prevalent neurologic findings were a complete or partial hemiplegia, convulsions and disturbances of consciousness. In three of the patients the picture was that of a complete or partial transverse myelitis. One patient presented both cerebral and spinal symptoms. Seventeen patients had pain as the initial symptom. Most of the neurologic involvements could be explained on the basis of interferences with the blood supply of the brain and spinal cord.

Schwartz, Shorey and Anderson⁸² report on a case of dissecting aneurysm of the aorta with a clinical neurologic picture of a transverse lesion of the spinal cord. The diagnosis was made prior to death. The cord lesion was due to myelomalacia secondary to vascular insufficiency, resulting from the presence of the aneurysm.

Hauser, Beyer, Jr. and Burger⁸³ report on a case of acute generalized platelet thrombosis occurring in a 20-year-old white woman. This disease, of unknown etiology, occurs in patients of either sex or color at ages ranging from nine to 66 years. The onset is acute and after a variable progressive course every case so far reported has died. The duration of the terminal illness varied from one week to two months. Clinical features include vague non-localizing symptoms, fever, purpura, anemia and thrombocytopenia and variable vague non-localizing neurologic and mental signs which may be fleeting and transient, although ultimately there is progression to delirium, stupor and coma before death. Mild icterus is present in about half the cases. These symptoms are due to widespread occluding platelet thrombi in the cerebral arterioles and capillaries. Petechiae and ecchymoses may be noted over the body surfaces. The urine may show blood cells and increased urobilinogen but no bile.

Wilson, Jr., Rupp, Riggs and Wilson⁸⁴ state that in a series of 542 cases in which an acute cerebral vascular accident was demonstrated at necropsy, the past medical history, clinical examination or autopsy revealed evidence of cardiocirculatory insufficiency in 451 (83 per cent). These findings suggest that systemic circulatory inadequacy plays an important part in the causation of cerebral vascular accidents. Preventive measures and therapy should be directed toward maintaining the general circulatory status at a maximum level.

PERIPHERAL NERVES

Diabetic Neuropathy and Its Prognosis. Despite the prevalence of diabetic neuritis, its etiology and its relation to the disturbance of sugar metabolism are little understood. In this respect the contribution by Epstein⁸⁵ is of some interest. In a series of 50 cases of diabetic neuropathy, 34 patients were female, 16 male. The average age at onset of the neuritis was 55.3 years;

only three patients were under 40 years of age. The average duration of diabetes prior to the development of neuropathy was 6.1 years. The onset was gradual in 42 cases. In only two cases was there an acute onset. In six cases the onset was subacute over a period of several weeks. Definite evidence of arteriosclerosis was present in 25 patients. None of the patients with arteriosclerosis showed any degree of neurologic improvement and some became distinctly worse. In the group of cases without demonstrable vascular disease, definite improvement was noted in practically every case. Complete recovery occurred in five. No differences in neurologic manifestations were found in the two groups. Muscular weakness in one or more extremities was observed in 23 cases. Pain was the cardinal symptom in 38. In less than half of them there was nocturnal exacerbation of pain. Usually the pain was localized in the feet and legs, but in seven the hands alone were involved. In one instance, pain was localized in the back and in another there was severe abdominal pain of segmental distribution. Parasthesiae alone were the major symptom in 11 cases and were present in all patients who had pain. Calf tenderness without objective sensory impairment was noted in ten cases. Alterations in the deep reflexes was the more common neurologic sign. The ankle jerks were absent in 30, the knee jerks in 35. The arm reflexes were diminished in ten. Deep sensibility was impaired more often than superficial sensation and occurred earlier than the latter disturbance. Atonic bladder was found in two cases and Argyll-Robertson pupils in one case. In 15 of 22 cases the spinal fluid protein was between 50 and 140 mg. per 100 cc. There were no other abnormal findings. A direct correlation was observed between the severity of the neurologic disturbance and the higher protein values. Only eight cases developed neuropathy when the diabetes was well controlled.

Serum Neuritis. Serum neuritis has been known for many years. The following abstract is of interest only as a reminder. Woolling and Rushton⁸⁶ report two cases of neuritis of the shoulder following injection of tetanus antitoxin. The condition may, at times, be confused with acute anterior polymyelitis, but the sequence of serum injection, serum sickness and localized pain and weakness developing over a one to three week period should permit the correct diagnosis. In the acute phase, treatment is aimed at reducing edema and pain; later, physical therapy is indicated. The prognosis is usually good; most patients recovered in four to six months. The occurrence of this condition should not be a contraindication to the administration of antitoxin. ³⁰

Halpern⁸⁷ states that the sensory pattern in radicular sciatica consists of a disturbance of superficial and deep sensibility. The superficial sensibility disturbance extended over the whole outside of the leg including the outer three toes and the hip. These unusual sensory boundaries were considered

to be due to a radiculitis if the first sacral root. Disturbed deep sensibility consisted of an occasional impairment of vibration sense and a constant disturbance of the sense of position in the outer three toes. This sensory pattern has been found in pure radicular sciatica as well as in spinal diseases superimposed on a segmental disturbance of sensibility with radicular participation.

Treatment of Polyneuritis. Menof⁸⁸ gave vitamin B12 to patients with alcoholic or diabetic polyneuritis in dosages of from 60 to 210 micrograms. The best results were achieved with the larger dose. In 11 cases, the results of treatment were encouraging. No untoward effects were experienced except for a little localized tenderness due to the large size of the intramuscular injection. Menof⁸⁹ also reports that in 9 of 11 cases of polyneuritis associated with chronic alcoholism or diabetic insipidus, dramatic improvement occurred following administration of vitamin B12. Equally satisfactory results were obtained in another series of 12 similar patients.

Thiele and Palm⁹⁰ state that intravenous injection of toxoid exerted no influence on the neurologic complications of diphtheria and failed to prevent the development of post-diphtheritic polyneuritis. In five cases small doses of toxoid (0.25 cc.) were given intraspinally. The favorable results indicated the effectiveness of this therapy. With small doses, there were no meningeal disturbances. Progressive disturbances in accommodation, swallowing, respiratory movements and other paralytic signs were the indications for intraspinal treatment.

Nielsen⁹¹ treated various forms of polyneuritis with BAL. Benefit was obtained in alcoholic polyneuritis, but only mediocre benefit in the polyneuritis of macrocytic anemia. Cases of the Guillain-Barré syndrome gave variable results. In some the response was dramatic, in others mediocre and there was no response in some. In the past few years some cases of the Guillain-Barré syndrome have shown porphyria. Therapy with BAL in these cases has been highly unsatisfactory. Nielson,⁹² in another article, reports on treatment of ten patients with Guillain-Barré syndrome with BAL. (British Anti-Lewisite 2:3:dimercaptopropanol). In nine of these, improvement was noted although in some patients it was not sustained. The criteria for selection of cases were polyneuritis with albumino-cytologic dissociation in the spinal fluid protein or polyneuritis with facial diplegia. The author suggests that the Guillain-Barré syndrome is basically a manifestation of a toxic interference with enzyme metabolism of ganglion cells which can be helped by BAL. He recognizes the presence of toxic porphyria in some cases of Guillain-Barré syndrome but at present is not able to relate the effects of BAL therapy to such occurrence.

Sagana and deOlaite⁹³ direct attention to the causal role of irritation of the gingival end branches of the trigeminus in the development of trigeminal

neuralgia and the onset of the crises. In a large group of patients between the ages of 36 and 82 years in whom neuralgia had lasted for 5 to 15 years, the point of maximal pain in the majority of cases was on either the upper or lower gums. Successful treatment consisted in infiltration of the gums with a 20 per cent phenol glycerin mixture which was injected at the point of maximal pain at the upper and lower gums. Neuralgia was controlled by the first infiltration in all cases. In three of six cases neuralgia recurred one or two years after infiltration but the pain was milder and it was controlled by a second infiltration. In two cases, cures lasting two and five years respectively followed one infiltration.

THE BASAL GANGLIA

The rather prevalent diseases of the basal ganglia remain major therapeutic problems. Unfortunately little has been added in the past year for furtherance of management of these cases.

Davis and Kunkle⁹⁴ encountered 14 cases of essential tremor in a general hospital in a ten-year period. The disease may begin at any age period and is characterized by a rhythmical tremor involving principally the hands, forearms, neck, head and face. The tremor is generally decreased or absent at rest and present on voluntary increase in muscle tonus. It is aggravated by emotion, fatigue, cold, caffeine and nicotine. Except for the increased terminal intention tremor which may interfere with feeding and writing, accuracy and coordination are little involved. There are no reflex or sensory changes. The tremor may progress for several years, then remain stationary and progress rapidly again in old age. In most cases the disorder can be traced through several generations frequently as a dominant characteristic. Both males and females are affected and either sex may transmit the disease. The proper treatment is explanation and reassurance that the condition will not be disabling. Phenobarbital and alcohol give symptomatic benefit. Scopolamine and trihexylphenidyl are of no benefit. The disease can be differentiated from Parkinsonism or lenticular degeneration by the absence of rigidity, the preservation of automatic associated movements, and rapid rhythmical alternating movements, the benign course and the familial history. It must be differentiated from tremors due to hyperthyroidism, cerebellar disease, general paresis and emotional tension.

Steinche⁹⁵ administered artane to 44 patients with various disorders of the central nervous system, but good results were obtained only in cases with extra-pyramidal motor disorders. The drug is of value chiefly in relaxing rigidity. In some cases, tremor, oculogyric crises and lethargy were favorably influenced. The side reactions are few and seldom distressing. Intoxication in the form of hallucination or confusion is as a rule seen only after protracted treatment with unnecessarily high doses. Treatment should

be started and stopped gradually. The optimal dose was 10 to 20 mg. daily varying individually. Combined treatment with one or more atropine group preparations may be advantageous. Patients with postencephalitic Parkinsonism tolerate and require larger doses than do those with other types of Parkinsonism. Special care must be exercised in patients who have had mental disorders.

Blumberg and Dattner⁹⁶ treated 23 patients with advanced Parkinsonism first with benadryl and then with theophorin. They were also maintained on belladonna derivatives and physiotherapy. The group was initially treated with 200 mg. of benadryl a day. Four patients rejected this in the first few days because of gastrointestinal upsets. Of 19 maintained on this dosage over one month, 13 reported some improvement, 3 noted no change and 3 felt worse. In seven, the improvement noted may have been ascribed to the sedative action of the drug. Six reported diminished tremor and increased motor power. Benadryl was then discontinued and after an adequate rest period, these same eight patients were started on from 100 to 200 mg. of theophorin a day. Transient gastrointestinal upsets were seen but did not necessitate discontinuing the medication. Sixteen patients stated they felt better, 14 described decreased rigidity and tremor. None felt worse. Objectively, however, definite evidence of improvement could be demonstrated in only a few. When theophorin was replaced by a placebo, loss of improvement was noted. Maximum improvement was reached within two or three weeks. The amount of subjective improvement in patients who had improved with benadryl was approximately the same as that obtained with theophorin. These drugs seem to act by potentiating the effect of the belladonna derivative. Theophorin in contrast to benadryl gave a somewhat more consistent improvement, without the complicating sedative action and without toxic side effects. In evaluating these results, it must be realized that the improvement noted was mostly subjective. Perhaps better effects could be obtained in less severe cases.

Dalsgaard-Nielsen⁹⁷ state the results of benadryl treatment were good in 15 cases of paralysis agitans. The dosage was 50 mg. three times a day, and in a few cases, 50 mg. four times a day. Side effects such as dizziness, general indisposition, weakness, and confusion occurred in only one case. In over half the cases, there was pronounced improvement in the general condition and in the bradykinesia, but the tremor was affected not at all by the treatment.

Cummings⁹⁸ states that since it has been shown that the liver and basal ganglia in hepatolenticular degeneration contain an excess of copper, and since BAL produces an increased urinary excretion of this element, the therapeutic effect of this drug was tried in four cases. In two cases improvement occurred; in one there was no improvement. The fourth patient

subjectively felt a little improved, but no real alteration was found. The improved patients had liver dysfunction and following treatment eventually urinary excretion of copper but not of amino acid nitrogen was lowered.

Yaskin⁹⁹ reviewed these agents in common use today in the treatment of Parkinson's syndrome and formulated some of the current concepts of the management of this condition. He states the optimum medication in any case of Parkinson's disease is a minimum for the given individual at any given time. There is often need for not only the combination of several agents but a relatively frequent change of medicinal agents when the effects of one have worn off. One must be continually on guard for toxic effects. In a good many cases it is well to discontinue all medications and, even at the cost of increasing rigidity and tremor, clear the system of drugs. It is well to bear in mind that some drugs frequently have a definitely unfavorable effect on this disease. This is especially true of the barbiturates. The following is a brief summary of medicinal agents presently in use:

Solanaceous Drugs. These have been used for many decades, and in the author's opinion are still the best. The chief of these is hyoscine (scopolamine) hydrobromide. He stresses that it is best to begin with small doses such as 1/200 grain (0.3 mg.) three times a day. In the course of time this may have to be increased to as high as 1/50 grain (1.2 mg.) three or four times daily. Other solanaceous preparations include the tinctures of belladonna or tincture of Hyoscyamus, 15 to 30 minims three times daily, rabellon 1 tablet three times daily, vinebol 1 tablet three times daily, and syntropan 50 mg. three or four times daily. All the solanaceous drugs have a tendency to produce blurring of vision, and occasionally, dryness of the skin and mucous membranes, and somnolence, and less commonly psychic changes. Many patients have been maintained in a state of usefulness by the use of hyoscine with periods of rest over a period of many years.

Antispasmodics. At present, the principal antispasmodic drugs include mephenesin (tolserol, myanesin) and artane. Mephenesin is administered in tablets gr. $7\frac{1}{2}$ to gr. 30 (0.5 to 2 gm.) three or four times daily. The intravenous use of mephenesin is neither practical nor desirable in the treatment of Parkinson's disease. Artane is administered in tablets gr. 1/64 to gr. 5/64 (1 to 5 mg.) three or four times daily. It is his clinical impression that these drugs are much more satisfactory in combination with the solanaceous agents than by themselves. The toxic effects of mephenesin include nausea and vomiting, and those of artane are nausea, vomiting, pruritus, and occasionally delirium.

Antihistaminics. These include (1) diphenylhydramine hydrochloride (benadryl) gr. $\frac{3}{4}$ to gr. $1\frac{1}{2}$ (50 to 100 mg.) three or four times daily. The toxic effects include excessive drowsiness and evidences of gastrointestinal

irritation. (2) Tripeleennamine hydrochloride (pyribenzamine) gr. $\frac{3}{4}$ to gr. $1\frac{1}{2}$ (50 to 100 mg.) three or four times daily. The toxic effects include states of delirium with hallucinations and paranoid trends. (3) Phenindamine tartrate (thephorin) gr. $\frac{3}{8}$ to gr. $1\frac{1}{2}$ (25 to 100 mg.) three or four times daily. The untoward symptoms include tension and restlessness, difficulty with sleeping, somnolence, and nausea and vomiting. (4) Methapyrilene hydrochloride (histadyl) gr. $\frac{3}{4}$ to gr. $1\frac{1}{2}$ (50 to 100 mg.) three or four times daily. The chief toxic effect appears to be drowsiness. It is his impression that these agents are useful largely as adjuncts to the solanaceous drugs, and should be used with considerable caution. It should be noted that the above-mentioned agents have been used only in recent years. It has become increasingly more apparent that it is the combination of the various agents that gives the patient most relief, and frequent changing of medication is of definite benefit.

Other Drugs. (1) The somnolence incident to the disease process as well as the drugs used may at times be partially relieved by the judicious use of the amphetamines (benzedrine) in doses from 5 to 1 mg. once or twice daily. (2) Insomnia occurring in postencephalitic Parkinson's disease or complicating psychotic reactions (toxic, structural or constitutional) are often a major therapeutic problem. I should like to stress the need for avoidance of barbiturates, bromides and opiates, and allied narcotic drugs. Paraldehyde, drams 1 to 4, every four to six hours, is felt to be the best agent. Occasionally, one has to resort to chloral hydrate (gr. 10 to 30) every six to eight hours. Better still is the avoidance of all drugs by placing the patient in a suitable hospital and using measures other than drug therapy to procure the disappearance of delirious reactions.

An extensive clinical and genetic study of paralysis agitans based on 194 probands has been presented by Mjönes.^{99a} The average age of onset is 49 ± 1.4 years. Tremor is the most constant and in some cases the only symptom. The incidence of formes frustes in the series is 20 per cent. Mental symptoms of "reactive" or "organic" type occur in approximately 40 per cent of the patients. The only tenable criterion for the diagnosis of hereditary paralysis agitans is the demonstration of secondary cases.

Hofer¹⁰⁰ reports that two or three daily injections of from 3 to 7 units of insulin along with a lump of sugar and a diet high in carbohydrates acted favorably on the muscular unrest in the early phases of chorea in 21 patients. The calming effect appears within a few days and is thought to be due to a central, possibly endocrine, improvement in neurologic regulation.

MULTIPLE SCLEROSIS

Within the past year there has been a considerable increase in interest in the problem of multiple sclerosis. Chiavacci, Hof and Polvan¹⁰¹ made a

statistical survey of 4,898 cases of multiple sclerosis in greater New York. The distribution of disease between the sexes was about equal and no predilection for any racial or national group was encountered save that the incidence in Negroes was only 1.4 in 10,000 while in whites it was 6 in 10,000. The age of onset was most frequent in younger adults. A relatively high number of patients showed a slow progression, but the majority showed a remittent course. The prognosis was better in cases with remissions. Early onset carried a better prognosis with regard to remission than onset in later life which was associated with a greater tendency to a slowly progressive or stationary course. Allergic conditions were not more frequent among patients with multiple sclerosis than among those with other diseases. Pregnancy, abortion, operations and injuries appeared to precipitate relapses. The age of death of patients with multiple sclerosis did not deviate much from the average mortality figures for the various decades, and most deaths occurred from intercurrent diseases.

Pratt, Compton and McAlpine¹⁰² report that in a series of 168 consecutive cases of disseminated sclerosis, there were 12 instances of one or more relatives being similarly affected. In an earlier series of 142 patients the family history was positive on eight occasions. Therefore, in a total of 310 cases the familial incidence was 6.5 per cent. The incidence of disseminated sclerosis in the siblings of 168 cases and in the parents of 310 cases is significantly higher than expected on the basis of a random distribution of the disease. This study supports the view that a genetic factor is present in multiple sclerosis and that there is evidence pointing to both a dominant and a recessive mode of inheritance. It is possible that the etiologic factors causing disseminated sclerosis may act more readily in the presence of an inherited disposition toward this disease.

Spicknall, Kurland et al.¹⁰³ found in a study of 20 patients with multiple sclerosis that skin reactions to *Brucella* antigens were no higher among multiple sclerosis patients than among patients with other diseases. Only 1 of 20 patients had a high *Brucella* agglutinin titer and the number of patients with low titers in both the multiple sclerosis patients and patients without this disease were of a degree and frequency similar to that experienced in routine serum surveys. This evidence fails to support the previously suggested impression that there is a strong and consistent relation between brucellosis and multiple sclerosis. Similarly, Eisele, McCullough and Beal¹⁰⁴ found no evidence of a relation between brucellosis and multiple sclerosis.

Campbell, Herdan, Tatlow and Whittle¹⁰⁵ studied the lead content of the soil in the homes of rural cases of disseminated sclerosis, all of whom had long been resident in their villages. The lead content was significantly

high in the soil of one village and the incidence of the disease in the two villages studied was abnormally great compared to findings in other areas. Also, the lead content of the teeth of cases of disseminated sclerosis has been found on the average to be significantly higher than in control groups. This evidence suggests that lead may play some part in the etiology of disseminated sclerosis. It is suggested that lead may interfere with some essential mineral, vitamin or enzyme reaction, and thus precipitate demyelination.

Gurthrie¹⁰⁶ states that generalized weakness, arm and leg weakness, dysarthria, decreased visual acuity and changes in visual fields occur in patients with multiple sclerosis as a response to total and partial body heating.

Yaskin, Spaeth and Vernlund¹⁰⁷ report that in 73 of 100 consecutive cases of multiple sclerosis, general neurologic symptoms were the earliest manifestations, while in 27, ocular symptoms were the initial complaint. The ocular manifestations included blurred, double or jumpy vision, difficulty in focusing or sudden or gradual loss of vision. Fifty-six cases showed ocular signs, 51 had changes in the optic discs, retrobulbar neuritis was present in 31 and in 14 it was the earliest manifestation.

Allison¹⁰⁸ studied a series of 40 unselected patients with disseminated sclerosis, all of whom lived in the same district and were seen for 20 years. Twenty-eight have died and 12 or 30 per cent survive. The average duration of the disease among the 28 dead patients was approximately 20 years. When the whole series is dead this average will naturally be still greater and the inclusion of the survivors at present indicates that the average for the whole series will be greater than 22 years. About 40 per cent of those now dead lived over 20 years. Longevity in patients surviving their fellows was usually purchased only at the expense of years of severe disablement. Coma often occurred as a terminal event in severely disabled patients and was sometimes preceded by frequent recurring epileptiform fits. Acute pulmonary complications, sepsis from bed sores, and toxemia from pyelitis are among the most frequent causes of death. Initial recovery of function usually follows a mild type of onset. With more severe symptoms only partial recovery of function is likely to occur. Many patients, however, with severe initial symptoms have survived long periods, though there has been some persistent disability from the onset. The tendency for symptoms to be repeated in subsequent relapses is observed—as is also the curious dissociation that exists between ophthalmoscopic appearance and visual acuity after acute retrobulbar neuritis. The almost stationary clinical condition exhibited by many of the survivors suggests that some self limiting or defensive process is at work. It is considered unlikely that in

these cases the disease is no longer active. Among the survivors, there is relatively little evidence of gross sphincter disturbance, loss of intellectual control or intellectual impairment. The preservation of these functions may be an important factor in the prognosis.

Weire and Schrader¹⁰⁹ analyzed the spinal fluids in 300 cases of multiple sclerosis. Cases were classified as acute which had shown new changes within the last three or four months (145 cases), and as chronic all without new changes (165 cases). Of the 145 acute cases, 104 showed pathologic changes in the spinal fluid but only 68 of the 165 chronic cases showed such changes. This suggests that the acuteness of the process is to a certain extent reflected in the spinal fluid. Acute cerebral processes showed a normal spinal fluid much more often than did the acute spinal or cerebrospinal processes. On the whole, the spinal fluid changes are not characteristic. Since the initial clinical symptoms are often atypical, the presence of spinal fluid changes may prove that they are of organic origin.

Muller¹¹⁰ reports that approximately half of 810 patients with disseminated sclerosis became ill before the age of 25 and less than 10 per cent at the age of 40 or over. To a great extent, the course and prognosis are determined by the age of the patient at the onset. In older patients the first bouts occur at shorter intervals than in younger patients. This is presumably true also with regard to subsequent bouts as long as the disease has not entered a steadily progressive stage. In older patients the disease frequently enters a steadily progressive stage as early as the first three bouts, i.e., one or more of the bouts become progressive whereas in younger patients this is uncommon. With more advanced age at the onset, it becomes increasingly common for the disease to enter a steadily progressive stage during the first years. The progressive bout is characterized by the successive intensity of some or all of the symptoms. Progression of the disease is characterized by increased motor disturbances. Spastic pareses are common, irrespective of the age of onset, but are oftener found at an advanced age. Cerebellar disturbances are more frequent at an early age of onset and are relatively uncommon at an advanced age. Progressive bouts occur earlier with advanced age of onset but the rapidity with which the disease progresses varies only unappreciably with age. Older patients become disabled after a shorter duration of illness than do those who were younger at onset. The mortality rate also appears to be higher for the older patients.

MacLean and Berkson¹¹¹ investigated 418 cases of multiple sclerosis who had been followed for at least ten years from the standpoints of whether the patient had become disabled to the extent of becoming unable to walk or engage in their ordinary work, and whether the patient was still alive.

For the entire group the five year survival rate was 93 per cent (95 per cent of normal) and for a ten year period 79 per cent (85 per cent of the normal expected rate). At the end of five years, 96 of an original 100 patients were living, and 64 were able to work and walk. At the end of ten years, 88 were living and 42 were able to walk and work. The rates obtained reflect a better outlook in respect to mortality and disability than is generally arrived. For the evaluation of any therapy, a five-year appraisal would appear to be the minimal time period necessary to deduce reliable conclusions.

Jonez¹¹² reports on 152 patients with multiple sclerosis, nearly all of whom showed some form of allergic sensitivity. Those with multiple food allergies appeared more spastic than those with other allergies. Histamine was given subcutaneously, intravenously, and by iontophoresis. The exacerbations of the disease were reduced in number under allergy management and histamine therapy, and the remissions lengthened. Some form of histamine therapy is indicated for the balance of the patient's life. The earlier treatment is started, the more successful it is. In chronic cases, varying degrees of improvement occur and continue as long as the patient continues treatment. Histamine therapy does not cure the disease but merely arrests symptoms. Patients who had been bed fast, were able to use a wheelchair or even become ambulatory. In others, all symptoms subsided and exacerbations were absent for over two years.

Aird¹¹³ administered sodium succinate intravenously to ten patients with multiple sclerosis and orally over prolonged periods to 22 patients. Subjective improvement was reported in 80 per cent and objective improvement was observed in approximately two-thirds of the patients by both methods of treatment. More prolonged follow-up observations on patients treated with the oral succinate have suggested that approximately one-half of them have been benefitted. Beneficial effects consisted of (1) improvement in dyssynergia, ataxia, dysmetria, balance and gait; (2) improvement in the flexor withdrawal reflex and clonus in some patients; and (3) subjective improvement in the appreciation of vibration and objective improvement in position sense and skin writing. Toxic effects were observed in one patient treated intravenously and in six patients given oral succinate. The later toxic reactions consisted of gastrointestinal and genitourinary effects and were not alarming. Three of these patients were able to continue treatment with benefit on reduced doses. Deterioration of the patient's condition on discontinuance of the succinate was observed in four instances. They all improved on resumption of the treatment. Recurrent episodes have been observed in three patients.

Arkin, Sherman and Weinberg¹¹⁴ treated a group of 42 patients with multiple sclerosis intensively with tetraethylammonium chloride for three

weeks. Although there was slight subjective improvement, it was concluded that tetraethylammonium chloride had no influence on the course of multiple sclerosis.

DEGENERATIVE DISEASES OF THE NERVOUS SYSTEM

The progress in the understanding of degenerative diseases stems from a better integration with other branches of internal medicine; from a more careful differential diagnosis between the degenerative diseases and those diseases more amenable to treatment, especially by neurosurgical means; and from advances in understanding of physiochemical and physiologic factors.

Strully et al.¹¹⁵ presented six cases of compression of the cervical cord in order to re-emphasize that the clinical syndromes caused by cervical cord compression may simulate various degenerative disorders of the spinal cord. The previous diagnoses of "degenerative cord disease," syringomyelia, multiple sclerosis, amyotrophic lateral sclerosis and combined systems disease had discouraged any active therapy. All, however, were slightly atypical syndromes. In all of the patients the course was progressive and the signs and symptoms could readily be accounted for by lesions below the foramen magnum. Signs and symptoms referable to the supracervical neuraxis were absent. In four patients there was an elevation of total protein in the spinal fluid. In five, there was osteoarthritic lipping and a narrow intervertebral space at the level of the lesion. In five, myelography of the cervical region of the spinal cord revealed a moderate or minimal defect at the level of the lesion. In all six patients, the pathologic process was a calcified, herniated intervertebral disc, associated with osteoarthritic lipping in such fashion as to produce a definite compression and angulation of the cord. Because of the nature of the lesions, surgical intervention was in all but one case limited to freeing the cord by section of the dentate ligaments. It is too early to report the final results of operation. Nevertheless, some improvement has already been evidenced in four patients even at this early date, from three to seven months after operation.

Bickerstaff¹¹⁶ described a family in which hereditary spastic paraplegia occurred widespread through three generations. Early or abortive forms of the disease were found in apparently normal members. Eighteen individuals were affected with the full blown syndrome while seven have shown signs of incipient disease. One child had a retrobulbar neuritis with papilledema which progressed to optic atrophy leaving diminished visual acuity but practically normal visual fields. Another child is probably affected in the same manner and two adults have been suspected of having swollen discs. Some members showed a picture similar to cerebral diplegia and in one case similar to amyotrophic lateral sclerosis. It is suggested that

this family gives further support to the view that the heredo-familial disorders of the nervous system are interrelated.

Barrett¹¹⁷ treated a white woman, aged 29, with spastic spinal paralysis with 3 grams of potassium nitrate per day, with considerable benefit. After three weeks, all spasticity was gone and the deep reflexes returned to normal. When treatment was discontinued, her symptoms recurred and were again promptly relieved when potassium was given.

Garland and Artley¹¹⁸ described a family showing a syndrome of spastic paraplegia, amyotrophy and pes cavus. The disease was transmitted as a Mendelian dominant. The pes cavus is not due to the amyotrophy and the amyotrophy is genogenic.

Bunting¹¹⁹ reported two cases of involvement of the posterior columns of the spinal cord in uncontrolled diabetes. No other etiologic factor except diabetes was found. Response to therapy, consisting of better control of the diabetes, parenterally administered multivitamins and liver extract in large doses has been gratifying. A plea is made to direct more attention to the nervous system, initially and in periodic follow-ups in all diabetics, thereby detecting neuropathies in the early phase during which therapy may be more beneficial.

Tom and Richardson¹²⁰ describe a case of islet cell tumor of the pancreas in which there developed a severe and fatal encephalopathy and myelopathy. The severe cerebral anoxic changes resulted in dementia, dysphagia, cortical visual disturbances and a terminal mild hemichorea. The unique and most interesting feature was a pronounced widespread degeneration of the ventral horn cells of the spinal cord, resulting in a paralysis and wasting of distal limb muscles. The name "Hypoglycaemic amyotrophy" might be suggested as a suitable one to describe the clinical and pathologic nature of the lower motor neuron lesion. It is unlikely that this rare effect of severe hypoglycaemia on ventral horn cells of the spinal cord will ever be encountered except in association with severe and prolonged cerebral changes.

Itallie and Graves, Jr.¹²¹ treated one case of amyotrophic lateral sclerosis of the subacute bulbar type for ten months with priscoline. The interruption of the patient's downhill course seemed prolonged and dramatic enough to suggest that the drug may have been of value.

Rabinovitch, Gibson and McEachern¹²² treated 107 patients with neuromuscular disorders with either wheat germ oil or wheat germ oil concentrate and sometimes with the addition of tocopherols. The cases were followed for periods varying from many months to 12 years. Thirteen cases showed definite improvement. Improvement was noted in two cases of atypical muscular atrophy. In 5 of 25 cases of progressive muscular dystrophy, symptoms were arrested and moderate to marked improvement

occurred. Three of five patients with menopausal muscular dystrophy showed remarkable improvement and three cases of dermatomyositis responded favorably.

DeWind and Jones¹²³ state that electrocardiographic abnormalities may often be expected as a part of the picture of dystrophia myotonica. These changes appear not to be related to any significant cardiac, physical or roentgen findings. Though unexplained, cardiomegaly is not infrequent. These findings cannot be attributed to coronary disease or to the quinine frequently administered in these cases, and it is suggested that the myocardium may itself be involved in dystrophia myotonica by the same process that affects the skeletal muscle.

Kiloh and Nevin¹²⁴ described five cases of progressive muscular dystrophy with early and predominant affection of the external ocular muscles. It is suggested that the term ocular myopathy be applied to these cases. Clinically ocular myopathy may begin at any time from infancy until late in life but the majority commence before the 30th year. A family history of ptosis or ophthalmoplegia is found in half the recorded cases. Ptosis is almost an invariable and nearly always the first sign. Rarely ophthalmoplegia appears first; usually it develops simultaneously with ptosis. The condition may or may not be symmetrical. Occasionally only one eye will be affected for many years. The onset and progression are both insidious. In fully developed ophthalmoplegia, a slight divergent squint is usual. Pupillary changes are not found. The facies in fully developed cases is characteristic with the forehead wrinkled, the head tilted backwards and the eyelids drooping and the eyebrows elevated. In a quarter of the cases various other muscles have been involved, especially the orbicularis oculi. In some cases, all the facial muscles are implicated. The muscles of mastication are not infrequently affected. Involvement of muscles supplied by spinal segments is found in 10 per cent of cases. All the neck and shoulder muscles may be weak; the sternomastoid wasted. The proximal muscles of the upper limbs may be involved. Usually the muscles of the pelvic girdle and legs are not involved. Ocular myopathy approximates most closely the Landouzy-Dejerine type of the disease. The pathologic changes in the muscles do not differ from those found in other types of progressive muscular dystrophy.

Hammes, Jr.¹²⁵ reports two cases of familial, and one of sporadic periodic paralysis. The disorder occurs more frequently in men (75 per cent). The onset is usually in adolescence although it may occur as early as six months and as late as the early fifties. The attacks commence, usually without premonitory symptoms, in one or several extremities and extend in an irregular fashion. There is no typical pattern, and the severity of the palsy may vary from mild weakness of one muscle group to a profound quadri-

plegia with respiratory paralysis. The pattern of paralysis may vary tremendously in extent and severity in the same individual during different attacks. Usually the paralysis appears during or after sleep. The muscles supplied by the cranial nerves are as a rule spared. The positive findings on examination are confined to a flaccid paralysis with diminution or loss of tendon reflexes in the involved areas. Sensation and mental functions are unimpaired. The disease tends to become less severe with age. Pregnancy has a favorable effect in reducing the frequency and severity of attacks. The mortality rate of about 10 per cent results from paralysis of the respiratory musculature. The attacks are accompanied by a drop in the serum potassium level. Treatment consists of prompt and liberal introduction into the body of potassium salts, and if necessary, the artificial maintenance of respiration. It is recommended that in any case of acute flaccid paralysis of undetermined origin a therapeutic test with potassium be made promptly. If the patient shows a positive reaction to a provocative test with high carbohydrate intake and epinephrine, carbohydrates should be avoided.

MYASTHENIA GRAVIS

The role of ACTH and cortisone in the treatment of various nervous diseases including myasthenia gravis and some interesting case reports form the substance of the year's progress.

Geddes and Kidd¹²⁶ state that myasthenia gravis has been considered rare below the age of ten, and, until recently, its occurrence in infants has passed unrecognized. The authors report the occurrence of transitory myasthenic symptoms with eventual complete recovery in 3 infants born of myasthenic mothers. From a review of the literature they conclude that neonatal myasthenia can be divided into two definite groups: true persistent congenital myasthenia gravis, so far reported only in children of nonmyasthenic mothers, and a transient myasthenia syndrome of the newborn, occurring in the infants of women with or without thymectomy, who have suffered from myasthenia gravis during their pregnancies. Before the advent of neostigmine (prostigmin) bromide it was customary to recommend therapeutic abortion to patients with myasthenia gravis. Now that more of such pregnancies are allowed to continue to term it is probable that cases of myasthenia syndrome of the newborn will be observed more frequently.

McKeever¹²⁷ describes, in addition to ten cases of congenital myasthenia gravis previously reported, another case of the disease occurring in a newborn child of a myasthenic mother. The myasthenic symptoms developed gradually and were clearly recognized by the second day of life. The diagnosis was proved by oral administration of neostigmine bromide and

the baby required no neostigmine after 15 days of life. The mechanism of the transient myasthenia is open to conjecture. Possibly there is an increase in cholesterinase in the infant which may be a reflection of an increased maternal circulating cholesterinase or possibly the increase in the infants' circulating cholinesterase developed in response to the neostigmine administered to the mother. The latter possibility seems more likely. No case of myasthenia gravis in infancy was observed prior to the introduction of neostigmine.

Perry¹²⁸ reported a case of diabetes mellitus in association with myasthenia gravis occurring in a 59-year-old Negress. The course was characterized by exacerbations and remissions of the myasthenic symptoms. The patient showed an excellent response to prostigmine. There was little if any improvement in strength with control of the diabetes alone.

Thibaudeau¹²⁹ reports on a four and one-half-year-old boy who developed myasthenia gravis. The onset was sudden with unexplained fatigue and ptosis of the upper lids. Within four months, the pseudoparalysis involved the muscles of the face, extremities and of the trunk. Despite daily oral administration of 8 to 12 tablets of neostigmine bromide, additional injections of 4.5 mg. of neostigmine methylsulfate per day and roentgen irradiation of the thymus, death resulted from cardiac failure during a myasthenic attack within six months of the onset of the disease. A degenerative inflammatory process in the thymus was demonstrated at autopsy.

Torda and Wolff¹³⁰ administered 500 mg. of ACTH to 15 patients with myasthenia gravis, and induced a significant partial remission of long duration in ten. Occurrence of remission could not be definitely established in four patients with very mild symptoms. During ACTH administration most of the patients became weaker and one patient died during the third day of treatment. The symptoms so developed seemed to be reduced in severity by the concomitant administration of potassium chloride.

Millikan and Eaton¹³¹ gave five patients suffering from myasthenia gravis one or more courses of injections of cortisone or ACTH. In every patient increased muscle weakness was observed toward the end of every course of treatment. Two patients had no improvement, one patient had slight transitory improvement, one patient had moderate transitory improvement, and one patient had marked transitory improvement after completion of the courses of cortisone or ACTH. The evidence is that cortisone and ACTH are of limited value in the treatment of myasthenia gravis.

Rider and Schulman¹³² state that octamethyl pyrophosphoramide, a stable and relatively potent anticholinesterase agent, can replace neostigmine in the treatment of some cases of myasthenia gravis. It has the advantage that two oral doses of from 9.5 to 18 mg. a day result in evenly maintained strength which is generally greater than the maximal strength

with neostigmine. There is a mutual potentiation of toxic side effects when neostigmine and octamethyl pyrophosphoramide are taken together. Since this is most marked in patients with severe myasthenia gravis, transfer from neostigmine to the new compound in such patients may be difficult or even impossible. Serum and red cell cholinesterase determinations are useful as a guide in dosage regulation during the period of transfer from neostigmine to octamethyl pyrophosphoramide. After the range of the maintenance dose is established, however, minor variations in the requirement of the new compound are not accompanied with changes in blood cholinesterase activity. After withdrawal of octamethyl pyrophosphoramide its therapeutic effect is greatly diminished within 24 hours, but the blood cholinesterase activity rises slowly to normal over a period of more than two months. There is no correlation between the severity of the disease or the neostigmine requirement on the one hand and dosage of octamethyl pyrophosphoramide on the other. Those patients who obtain little benefit from even large amounts of neostigmine will probably get little additional benefit from the new drug.

Atkinson, Jr.¹³³ treated a woman, aged 42, with myasthenia gravis for three years with neostigmine. In spite of gradual increase of the dose, the patient was bedfast and had great difficulty in swallowing and breathing. Two mg. of tetraethyl pyrophosphate were given before neostigmine therapy, and four hours after the last dose of neostigmine. After the second dose of tetraethyl pyrophosphate, the patient began to feel stronger. Neostigmine was continued as often as necessary, and the dose of tetraethyl pyrophosphate was increased by 1 mg. a day until she was given 6 mg. twice a day. The dose was then increased by one-half mg. a day, and when 7 mg. twice a day were given, the patient was able to discontinue the neostigmine. When a dose of 8.5 mg. twice a day was reached, the patient was able to lead an almost normal life. She was given 1.75 mg. of atropine after each dose of tetraethyl pyrophosphate. The only unpleasant side effect was an unusually large amount of saliva.

HEADACHE

Headache remains a major diagnostic problem in the practice of nearly all branches of medicine and surgery. After screening those cases due to known structural and chemical causes, there remain millions of people who have recurrent headaches of more or less unknown etiology. It seems that an honest effort is being made to explore this problem from various psychobiologic standpoints, so that a great many patients are helped, either by physical, chemical or psychologic methods or by their combined use. The following articles throw some additional light on these problems.

Patrikons¹³⁴ states there is no difference in respect to the clinical features

of ophthalmoplegic migraine with a migrainous basis and those of the condition with a non-migrainous basis. The ophthalmoplegic seizures are usually much longer than those of common migraine. The cranial nerve affected is not always the same in successive seizures. Other cranial nerves than the oculomotor may be involved. Motor (7th), sensory (5th or 8th) or vegetative (10th) nerves may be affected. In some cases, the spinal fluid is altered which supports the hypothesis of the vaso-exudative etiology of the condition. Factors that might initiate this vaso-exudative process in the brain appear to be multiple. In some cases the cause appeared to be psychic, in two cases it was chemical—a wasp sting. In two cases the ophthalmoplegic migraine developed after a lesion of the third cranial nerve due to poliomyelitis virus, the lesion having apparently created a “thorn” which acted as an irritant to produce subsequent attacks. In another case, the condition developed after an acute meningeal reaction, this lesion having apparently created another “thorn”. Psychotherapy, when applied at the onset of the attack, is an efficacious therapeutic method.

Fuchs and Blumenthal¹³⁵ state that although ergot is a potent and effective agent in the treatment of the migraine attack, toxic reactions may occur from its use. Two such cases are reported. A woman, aged 48, 30 to 40 minutes after taking two cafergone tablets developed emesis, precordial pain, palpitations, numbness of the extremities and cramps in the muscles of both thighs. Her lips and nailbeds were cyanotic, pulses were barely perceptible and the extremities were cold. The symptoms remained severe for four hours but gradually cleared within a day. Subsequently, the patient was able to take dihydroergotamine or ergotamine tartrate without untoward effects. One other patient, a woman aged 41, following subcutaneous administration of 1 cc. of dihydroergotamine developed substernal pain which did not subside with rest. An electrocardiogram showed significant changes but returned to normal within three months. In order to prevent toxic reactions, overdosage should be carefully avoided; malnutrition and hypertension are conditions that should lead to further restraint in the use of ergot alkaloids.

Brentan¹³⁶ reports that dramamine (dimenhydrinate) proved effective in seven cases of migraine. By using the drug at the onset of prodromal symptoms, all manifestations of the migrainous headaches were abated and the patients were able to resume normal activities almost immediately. All patients had previously received the other usual medications with slight or no relief.

Gans¹³⁷ suggests that the cause of migraine attacks should be sought in too deep or too long sleep. Treatment consists in “sleep rationing,” a method of regulating sleep which sets out to prevent such excessive sleep. This treatment is supported by dietetic and physical auxiliary measures.

MISCELLANEOUS

The following articles represent unique conditions and case reports.

Brain et al.¹³⁸ described four cases of subacute *cortical cerebellar degeneration*. In all cerebellar symptoms developed fairly rapidly in patients past middle age and contributed to their death at intervals of three and a half to seven months from the onset of the disease. Progressive dementia appeared soon after the onset of the cerebellar symptoms in three. Diplopia of the cerebellar type was present in all and was an early symptom in three. Cramp-like pains in the legs heralded the onset of cerebellar symptoms in two cases. In three of the cases there was also degeneration of the long tracts of the spinal cord (direct spino-cerebellar in all, pyramidal in one and dorsal columns in the other two). In these three cases there was also carcinoma, of the bronchi in two and of the ovary in one. A review of the literature shows a high correlation of carcinoma with subacute cortical cerebellar degeneration. Of cases which have run their course in two years, more than two-thirds have had carcinoma, although this has not always been clinically evident. The more chronic forms of cerebellar degeneration show no such correlation. In considering the pathogenesis of the disease, emphasis is laid on the special vulnerability of the Purkinje's cells to extrinsic poisons or intrinsic metabolic disturbances, but no explanation is found in this for the rarity of the disease. Hallgren's^{138a} study of *specific dyslexia (congenital word-blindness)* based on 276 cases indicates that, at least in boys, there is a direct association between speech defects and specific dyslexia.

The calculations made have failed to prove statistically that there is a direct association between left-handedness and specific dyslexia. The incidence of left-handedness in his series is, however, consistently higher in the affected than in the unaffected children. A rough estimation of the incidence of specific dyslexia in the normal population gives an approximate figure of 10 per cent.

Gay¹³⁹ gave dimenhydrinate (dramamine) in doses of from 50 to 100 mgms. every four hours to 63 patients with various types of *dizziness* of labyrinthine as well as of central origin. Seventy-five per cent of the patients were greatly improved after taking the drug, but many had to continue maintenance doses to remain symptom free. The benefits derived from the drug showed that it should be given to all persons with disturbed balance before recourse to surgical procedures.

Slepian and Hornby¹⁴⁰ state that neurologic complications associated with *hereditary deforming chondrodysplasia* are rare, 19 cases being found in the literature. Two new cases occurring in brothers are described. Males are most frequently involved. The spinal cord was involved in ten, the

sciatic nerve in six, the peroneal nerve in two and the brachial plexus and ulnar nerve in one case each.

Stone¹⁴¹ reports on three brothers who have each had two or more attacks of *peripheral facial palsy*. One of the brothers also had two attacks of ophthalmic migraine with external ophthalmoplegia. The father of these patients had an attack of peripheral paralysis of the left facial nerve in 1940. This was three years ago and one year after the facial paralysis experienced by the first and second patients, and one year before that of the third patient. The author cannot state whether all these paralyses are due to hereditary or familial factors.

Kennedy et al.¹⁴² report on 15 cases of grave paralysis following the use of *spinal anesthesia*. In addition, aseptic, purulent and chronic adhesive meningitis have been reported to occur after spinal anesthesia. Even cerebral injuries have been reported. Convulsive disorders with or without hemiparesis have occurred from 5 to 15 days after the anesthesia, and encephalitis has been observed. Cranial nerves and the anterior and posterior roots and peripheral nerves have also been affected as well as the cord. The neurologic complications of spinal anesthesia occur in the regions of the nervous system closest to the site of injection. The authors feel that spinal anesthesia should be reserved for cases in which local or general anesthesia is unsuitable, since paraplegia is too large a price for the patient to pay in order that the surgeon may have a relaxed operative field.

Jewsbury¹⁴³ states that *temporary insensitivity to pain* may occur in states of profound emotion, hysteria or hypnosis, also in some cases of postencephalitic personality disorders and in some forms of psychosis. Persistent insensitivity to pain may occur with mental deficiency, usually in direct proportion to the defect. Insensitivity to pain has also been described with various cerebral lesions involving the major hemisphere, particularly the parietal lobe. In rare cases, insensitivity to pain occurs as a congenital abnormality associated with little or no mental defect. In such cases there may be a personal or family history of epilepsy, personality disorder or tendency to left-handedness. Three cases of congenital insensitivity to pain in adults of ordinary intelligence are described. In spite of their indifference to physical discomfort, the subjects had no difficulty in distinguishing different kinds or degrees of pain stimuli. In one case, a child was seemingly indifferent to painful stimuli until the third year of his life. Congenital insensitivity to pain resembles an agnosia and may result from a faulty development of cortical or cortico-thalamic pathways or faulty integration of nerve impulses within the major hemisphere.

Martin¹⁴⁴ described four cases in which *attacks of laughter* occurred in association with organic cerebral disease. The episodes of laughter are considered to be fits comparable with Jacksonian seizures. The patient's

emotional state at the time of such an attack is not that appropriate to laughter. The mirth is a "sham." In every case in which there were indications of the site of the lesion it was so placed that it might affect the hypothalamus, and it is likely that the motor center for laughter is situated in or near the hypothalamus. The center which discharges is a motor center and not one exciting emotion. Usually the attacks are of dire omen in that they are usually followed by severe vascular disorders.

Johnson and Chalgren¹⁴⁵ state that neurologic symptoms occur in at least $\frac{3}{4}$ of all cases of *polycythemia vera* and in $\frac{1}{3}$ is the most important complaint. The most common symptoms are nonspecific and include headache, vertigo, fatigue and weakness. Visual disturbances, paresthesias and vague aches and pains are frequent. These symptoms combined with many other complaints often lead to an erroneous diagnosis of neurosis. Occasionally a confusional type of psychosis may develop. Many of these symptoms disappear when the blood values are restored to normal. Over one-fourth of the patients with neurologic symptoms present objective neurologic findings. These are usually focal in character and are due to vascular thrombosis. Hemiplegias are most common, but extrapyramidal syndromes may also occur. The cerebral lesions occur in multiple areas of the brain, and repeated thromboses are followed by more or less complete recovery. In some cases the lesions appear to be progressive and may be mistaken for brain tumor, especially if increased spinal fluid pressure with choked disc is present. Diencephalic lesions are occasionally found. Paresthesias are common complaints, but actual peripheral neuritis is rare.

Ethelberg¹⁴⁶ states that so-called *cataleptic attacks* or accesses of general limpness developed in two cases of depressed fracture which made an impression upon the lateral surface of the frontal lobe corresponding to the anterior part of the motor cortex (areas 6 and 8). Sometimes the attacks were associated with blunting or loss of consciousness. They are considered to be one of the epilepsies and the attacks have been described as "inhibitory epilepsy." However, the term *chalcastic fit* is proposed as being more descriptive.

de Moragas¹⁴⁷ calls attention to a neurologic syndrome that may occasionally appear in *infants* immediately after birth, together with *jaundice*. About 20 cases were observed. The syndrome usually appeared in the second child and only rarely in the first-born child. Usually the infant and the father were Rh positive whereas the mother was Rh negative, but in other cases the Rh incompatibility could not be proved. Most frequently, the neurologic syndrome consisted of choreoathetosis, extrapyramidal hypotonia or hypertonia, ataxia and dysarthria. Treatment which was prolonged consisted of muscular relaxation exercises and administration of pyridoxine (vitamin B6), pantothenic acid and, in some cases, magnesium

sulfate and drugs with an effect similar to that of caramiphen hydrochloride (panparnit). In cases of this type the late sequelae were mild, consisting of moderate ataxia, dysarthria and moderate psychomotor instability. These children were socially normal and able to get an education. In some cases the syndrome consisted of oligophrenia, oculogyric crises, convulsions, tremor, dysmetria and adiadokokinesia. The neurologic sequelae were uncontrollable in cases of this type.

Frantz¹⁴⁸ reports that orally given *mephenesin* (tolserol) was well tolerated over a seven-month period in 23 children of a test group of 27 subjects with *infantile cerebral palsy*. Vertigo, nausea, vomiting, instability and listlessness were undesirable side effects noted in cases receiving doses up to 2 gm. Vertigo was in most cases easily controlled by change in dosage. No undesirable results were manifest in blood and urine studies. Children with spasticity and rigidity did respond satisfactorily; of 16 athetoid children, 14 demonstrated beneficial results. Children with intense athetosis seem to have a favorable response to mephenesin more consistently than other groups.

ACTH AND CORTISONE

Within the past year, ACTH and cortisone have been used in the treatment of many diseases, including those of the nervous system. Reference has already been made to some of this work. Additional contributions are here recorded.

Shy, Brendler et al.¹⁴⁹ treated 12 patients with various *neuromuscular disorders* with cortisone. In 2 patients with dystrophia myotonica, the myotonic response was completely abolished by cortisone therapy during the period of treatment. Improvement in the dystrophic state was doubtful. One patient with generalized lupus erythematosus and an acute dystrophic process in the skeletal muscles showed marked improvement of the constitutional state. There was, however, no improvement in muscle power. Another patient, with less severe manifestations of this disorder improved dramatically, and muscle power returned to normal. One patient with juvenile muscular dystrophy with collagen changes and two patients with motor neuron disease were unimproved by cortisone therapy. One patient with myasthenia gravis was made worse by cortisone therapy but returned to his previous status on discontinuance of treatment. Two women with menopausal muscular myopathy showed decided improvement while being treated with cortisone. One man also improved on the same therapy and dosage, but another man failed to improve. This condition in women previously had been found to respond to wheat germ oil therapy but with a longer time lag.

Jonsson and Von Reis¹⁵⁰ gave ACTH to four patients with *disseminated*

sclerosis. The total dosage was 300 mg. Following treatment, two patients showed increased motility and muscle strength, decreased ataxia and better ability to stand walk. A third patient with symptoms of longer duration showed limited improvement. The fourth patient with chronic advanced symptoms showed no practical change. The best and quickest results were obtained in regions which had recently been the seat of progressive symptoms. The first patient had a relapse and was dying when he was given an abridged ACTH treatment and 900 mg. of cortisone. Symptoms decreased rapidly. Seven cases received cortisone. Improvement was not as pronounced as with ACTH.

Rothendler¹⁵¹ reports a case of *Bell's palsy* in a 59-year-old woman which was treated with cortisone. A remarkable and rapid improvement noticed within 48 hours could hardly be attributed to spontaneous recovery. It is suggested that cortisone causes a rapid reduction in the congestion of the nerve sheath in the bony canal. Further study of the effect of the drug in this condition is warranted.

Shy and McEachern¹⁵² treated 45 patients with various neurologic disorders with cortisone or ACTH. In three cases of myotonia dystrophica, the myotonia was abolished during treatment with cortisone, but it returned when treatment was discontinued. No improvement was noted in the dystrophic process. In a case of myotonia congenita the severe generalized myotonia was abolished during ACTH treatment, but it returned during treatment with DCA. The myotonia decreased again with cortisone. Three cases of *myasthenia* gravis received cortisone; in two, the myasthenia became worse during treatment. Symptoms returned to the previous level when the drug stopped, but there was no rebound improvement. In one case a profound state of muscle dystrophy occurring during the course of acute disseminated lupus erythematosus responded remarkably to cortisone, but, in another, the muscle weakness was unaffected by either ACTH or cortisone although the constitutional symptoms were abolished. Three cases of amyotrophic lateral sclerosis and of peripheral motor neuropathy were uninfluenced by cortisone. No improvement was noted in three cases of progressive muscular dystrophy of the childhood type. Seven out of eight cases of menopausal muscular dystrophy have shown striking improvement with cortisone but maintenance dosage is necessary.

Shy and McEachern¹⁵³ state that a *myopathy* affecting proximal girdle muscles (hips and shoulders) can be distinguished from other myopathies of late onset by a typical pathologic picture. This condition occurs in the post-climateric period, predominantly in women. Some patients have been treated over long periods of time with wheat germ oil with temporary relief for periods up to three years. The patients have also responded well to the administration of cortisone acetate.

REFERENCES

- ¹ Van Zebe, W.: Difficulties and possibilities in the diagnosis of tuberculous meningitis. *Maandschr. v. kindergeneesk.* 18:45, 1950.
- ² Portella, A.: The tryptophan test on the CSF in tuberculous meningitis. *Rassenga internaz. clin. e terap.* 30:299, 1950.
- ³ Urban, N.: Potassium and sodium content of the CSF in tuberculous meningitis. *Monatsschr. Kinderh.* 98:145, 1950.
- ⁴ Tapie, J., Monnier, J., Delaude, A., and Gontier: Chloride determination in the CSF for the diagnosis and conduct of treatment of tuberculous meningitis. *Presse méd.* 58:809, 1950.
- ⁵ Ewerbeck, H.: Electrophoretic study of the serum proteins in tb meningitis and miliary tb; effect of streptomycin. *Klin. Wchnschr.* 28:638, 1950.
- ⁶ Van Beek, C., Haex, J. C., Smit, A., and Van Veen, G. R.: Aspiration liver biopsy in the early diagnosis of tb meningitis. *Geneesk. gids.* 28:515, 1950.
- ⁷ Aubry, G., Boulard, C., Portier, A., and Pellicier, Y.: Latent tb meningitis discovered by encephalography during systemic examination on account of retarded development. *Algérie méd.* 65:543, 1950.
- ⁸ Fouguet, Jr.: The early diagnosis of tuberculous meningitis. *Semained. Hôp. de Paris.* 26:844, 1950.
- ⁹ Auersbach, K. and Von Bergmann, I.: Tuberculous meningitis after immunization against typhoid. *Ztschr. klin. Med.* 145:346, 1949.
- ¹⁰ Perry, T. L.: Natural history and pathogenesis of miliary and meningeal tuberculosis in children. Analysis of 163 cases. *Pediatrics.* 5:988, 1950.
- ¹¹ Lincoln, E. M. and Kirmse, T. W.: Streptomycin-promizole therapy of miliary and meningeal tuberculosis in children. *Am. Rev. Tuberc.* 61:159, 1950.
- ¹² Russell, S. J. M. and MacArthur, P.: Treatment of tuberculous meningitis with streptomycin. *Lancet.* 1:59, 1950.
- ¹³ MacCarthy, D. and Mann, T. P.: Tuberculous meningitis in children. *Lancet.* 1:341, 1950.
- ¹⁴ Smith, H. V. and Vollum, R. L.: Effects of intrathecal tuberculin and streptomycin in tuberculous meningitis. An interim report. *Lancet.* 2:275, 1950.
- ¹⁵ Dubois-Manne, R.: Clinical observations on the treatment of tb meningitis, collected since November 1946. *Semainede hôp. de Paris,* 26:3102, 1950.
- ¹⁶ Gonin, A. et al.: Contribution to study of treatment and of prognosis of tuberculous meningitis. *J. méd. Lyon* 31:237, 1950.
- ¹⁷ Bertoye, P. et al.: Brief considerations on treatment of 34 patients with tuberculous meningitis. *J. méd. Lyon,* 32: 457, 1951.
- ¹⁸ Chaptal, J., Brunel, D. et al.: Results of 18 months of streptomycin therapy of tuberculous meningitis. *Arch. franç. pédiat.* 6:561, 1949.
- ¹⁹ Rossi, E.: Present status of therapy of tuberculous meningitis and results at Children's Hospital in Zurich. *Helvet. paediat. acta.* 5:27, 1950.
- ²⁰ Choremis, C., Zervos, N. et al.: Further observations on application of streptomycin in treatment of tuberculous meningitis. *Acta tuberc. Scandinav.* 25:8, 1950.
- ²¹ Behr, W.: Treatment of miliary tb and tb meningitis with streptomycin and thiosemicarbazone. *Deutsche Gesundh. Wes.* 5:1630, 1950.
- ²² Brainerd, H. D. and Eagle, H. R.: Effect of streptomycin on tuberculous meningitis. *Ann. Int. Med.* 33:397, 1950.
- ²³ Calnan, W. L., Rubie, J., and Mohun, A. F.: Tuberculous meningitis treated with streptomycin. *Brit. M. J.* 1:794, 1951.

- ²⁴ Bunn, P. A.: Two year follow-up report of patients with miliary and meningeal tuberculosis treated with streptomycin. *Am. J. M. Sc.* 219:127, 1950.
- ²⁵ Lassen H. C. A. and Neukirch, F.: Streptomycin treatment of tuberculous meningitis and miliary tuberculosis. *Ugesk. f. læger* 113:623, 1951.
- ²⁶ Shonenberg, H.: Constitutional changes in chronic tuberculous meningitis. *München. med. Wehnschr.* 92:343, 1950.
- ²⁷ McKay, R. J. et al.: Reactions to intrathecal streptomycin. *J.A.M.A.* 147:818, 1951.
- ²⁸ Howard, J. E. et al.: Hydrocephalus in Tuberculous meningitis. *Rev. chilena de pediat.* 21:377, 1950.
- ²⁹ Bünger, P. and Geiger, W.: Some neurological syndromes in tb meningitis treated with streptomycin. *Deutsche. Ztschr. Nerven.* 164:427, 1950.
- ³⁰ Bünger, P.: Pathogenesis of endocrine symptoms in tuberculous meningitis. *Klen. Wickers.* 29:338, 1951.
- ³¹ Appelbaum, E. and Nelson, J.: Streptomycin in the treatment of influenzae meningitis. A study of 90 cases with 96.6 per cent recovery. *J.A.M.A.* 143:715, 1950.
- ³² McMorro, K. J. and Top, F. H.: Treatment of H. influenza B meningitis. *Pediatrics.* 5:452, 1950.
- ³³ Prather, G. W. and Smith, M.: Chloramphenical in the treatment of Hemophilus influenzae meningitis. *J.A.M.A.* 143:1405, 1950.
- ³⁴ McCrumb, Jr., F. R. and Hall, H. E. et al.: Treatment of Hemophilus influenzae meningitis with chloramphenical and other antibiotics. *J.A.M.A.* 145:469, 1951.
- ³⁵ Swift, P. N. and Bushby, S. R. N.: H. influenzae meningitis treated with polymixin. *Lancet.* 2:183, 1951.
- ³⁶ Simpson, W. H. and Holley, H. L.: Pneumococcal meningitis. *Am. Pract. & Digest. Treat.* 2:486, 1951.
- ³⁷ Nemir, R. L. and Israel, J.: Pneumococci meningitis in infants and children. *J.A.M.A.* 147:218, 1951.
- ³⁸ Hoyne, A. L. and Herzon, H.: Streptococcic viridans meningitis. *Ann. Int. Med.* 33:879, 1950.
- ³⁹ Teng, P.: Further experiences in treatment of septic meningitis with bacitracin. *Arch. Neurol. & Psychiat.* 64:861, 1950.
- ⁴⁰ Myerson, R. M.: Meningitis during gold therapy. *J.A.M.A.* 143:1336, 1950.
- ⁴¹ Greenberg, M., Siegel, M., and Magee, M. C.: Poliomyelitis in New York City 1949. *New York J. Med.* 50:1119, 1950.
- ⁴² Hargreaves, E. R.: Poliomyelitis in Cornwall in 1949. *Brit. M. J.* 1:879, 1950.
- ⁴³ Mackenzie, E. F. W.: Poliomyelitis and public water supplies. *Pub. Health.* 64:21, 1950.
- ⁴⁴ MacLean, F. S.: How is poliomyelitis spread? An epidemiological study. *New Zealand M. J.* 49:652, 1950.
- ⁴⁵ Behrend, R. C. and Hansen, K.: Clinical-epidemiological studies on the 1947 poliomyelitis epidemic at Hamburg. I. Mode of spread of poliomyelitis in Greater Hamburg before and during the epidemic. II. Significance of temporarily variable factors for the course and character of the epidemic (Participation of various virus strains in the development and appearance of epidemics). *Ztschr. Hyg.* 132:477, 1951; *Deutsche Ztschr. Nerven.* 165:488, 1951.
- ⁴⁶ Lenarsky, M., Pass, R. L. and Seassor, H. E.: Epidemic poliomyelitis; Review of 526 cases. *Am. J. Dis. Child.* 82:160, 1951.
- ⁴⁷ McLeod, W. J.: Poliomyelitis and diphtheria immunization in Belfast. *Brit. M. J.* 1:736, 1951.

- ⁴⁸ Goerke, L. S.: Poliomyelitis: Precipitation by injections. *California Med.* 74:383, 1951.
- ⁴⁹ McCloskey, B. P.: Relation of prophylactic inoculations to onset of poliomyelitis: Study of 620 cases in Victorian epidemic of 1945. *M. J. Australia* 1:619, 1951.
- ⁵⁰ Anderson, G. W. and Skaar, A. E.: Poliomyelitis occurring after antigen injections. *Pediatrics.* 7:741, 1951.
- ⁵¹ Sedallian, P. and Gaillard, L.: Development of Paralysis in two stages in Heine-Medin disease. *J. Méd. Lyon.* 32:331, 1951.
- ⁵² Lans, H. S., Stein, I. F., Jr. et al.: Potassium deficiency in bulbar poliomyelitis. *J.A.M.A.* 146:1017, 1951.
- ⁵³ Cook, C. D., Hartmann, J. R. et al.: Gastrointestinal lesions in acute bulbar poliomyelitis. *Pediatrics.* 7:415, 1951.
- ⁵⁴ Neuman, P. H.: Radicular manifestations in poliomyelitis. *Deutsche. med. Wchnschr.* 75:107, 1950.
- ⁵⁵ Albrecht, R. M. and Locke, F. B.: Effect of physical activity on prognosis of poliomyelitis. *J.A.M.A.* 146:769, 1951.
- ⁵⁶ Brahdy, M. B. and Katz, S. H.: Effect of transportation on seventy cases of acute poliomyelitis. *J.A.M.A.* 46:772, 1951.
- ⁵⁷ Zellweger, H. and Morf, H.: Neurosympathetic disturbances in poliomyelitis: trophic disturbances. *Helvet. paediat. acta.* 5:434, 1950.
- ⁵⁸ Coffee, A. T. and Paul, W. D.: Second attacks of acute anterior poliomyelitis. *Neurology.* 1:401, 1951.
- ⁵⁹ Hoyne, A. L. and Lipton, I.: Second attacks of poliomyelitis. *J.A.M.A.* 146:707, 1951.
- ⁶⁰ Sarnoff, S. J. et al.: Electrophrenic respiration in poliomyelitis. *J.A.M.A.* 143:1383, 1950.
- ⁶¹ Smith, E., Graubard, D. J. et al.: Clinical management of acute poliomyelitis. 144:213, 1950.
- ⁶² Geisler, W. O., Mustard, W. T., and Anglin, C. S.: The treatment of pain and 'spasm' in poliomyelitis with 'priscoline'. *Canad. M.A.J.* 63:60, 1950.
- ⁶³ Appelbaum, E. and Saigh, R.: Aureomycin in the treatment of poliomyelitis. *J.A.M.A.* 143:538, 1950.
- ⁶⁴ Fox, M. J. and Hornberger, Jr., E.Z.: Phenosulfazole (darvisul) in acute poliomyelitis. *J.A.M.A.* 143:535, 1950.
- ⁶⁵ Binet, L. et al.: Cortin (adrenal extract) in treatment of poliomyelitis. *Progr. méd., Paris.* 77:563, 1949.
- ⁶⁶ Steegman, A. T. and Davis, H. V.: Anoxic encephalopathy following poliomyelitis. *Arch. Neurol. & Psychiat.* 63:774, 1950.
- ⁶⁷ Anderson, I. M. and Morris, D.: Encephalopathy after combined diphtheria pertussis inoculation. *Lancet.* 1:537, 1950.
- ⁶⁸ Bernstein, T. C. and Wolff, H. G.: Involvement of the nervous system in infectious mononucleosis. *Ann. Int. Med.* 33:1120, 1950.
- ⁶⁹ Mulder, D. W.: Western equine encephalitis. *Dis. Nerv. System.* 12:259, 1951.
- ⁷⁰ —, Parrott, M., and Thales, M.: Sequelae of Western equine encephalitis. *Neurology.* 1:318, 1951.
- ⁷¹ Hullinghorst, R. L., Burns, K. F., et al.: Japanese B encephalitis in Korea. *J.A.M.A.* 145:460, 1951.
- ⁷² Orbison, J. A., Reeves, N. et al.: Amebic brain abscess. *Medicine.* 39:247, 1951.
- ⁷³ Brown, I. A. and Peyton, W. T.: Brain tumors simulating meningitis. *J. Neurosurg.* 8:459, 1951.

- ⁷⁴ Bolus, M. and Wilkinson, J. S.: Aureomycin and chloromycetin in therapy of Herpes zoster. *North Carolina M.J.* 11:80, 1950.
- ⁷⁵ Webster, J. E., Dolgoz, S., and Guidjian, E. S.: Spontaneous thrombosis of the carotid arteries in the neck: *Arch. Neurol. & Psychiat.* 63:942, 1950.
- ⁷⁶ Fisher, M.: Occlusion of the internal carotid artery. *Arch. Neurol. & Psychiat.* 65:346, 1951.
- ⁷⁷ Conley, J. W. and Rand, C. W.: Spontaneous subarachnoid hemorrhage occurring in noneclamptic pregnancy. *Arch. Neurol. & Psychiat.* 66:443, 1951.
- ⁷⁸ Biemond, A.: Thrombosis of the basilar artery and the vascularization of the brain stem. *Brain*. 74:300, Part III, 1951.
- ⁷⁹ Steegman, A. T.: Primary pontile hemorrhage. *J. Nerv. & Ment. Dis.* 114:35, 1951.
- ⁸⁰ Epstein, A. W.: Primary massive pontine hemorrhage. *J. Neuropath. & Exper. Neurol.* 10:426, 1951.
- ⁸¹ Moersch, F. P. and Sayre, G. P.: Neurologic manifestations associated with dissecting aortic aneurysm. *J.A.M.A.* 144:1141, 1950.
- ⁸² Schwartz, G. A., Shorey, W. K. and Anderson, N. S.: Myelomalacia secondary to dissecting aneurysm of the aorta. *Arch. Neurol. & Psychiat.* 64:407, 1950.
- ⁸³ Hauser, A., Beyer, A., Jr., Burger, R. A.: Encephalopathy associated with acute diffuse platelet thrombosis. *Arch. Neurol. & Psychiat.* 65:672, 1951.
- ⁸⁴ Wilson, G., Rupp, C., Jr., Riggs, H. E., and Wilson, W. W.: Factors influencing the development of cerebral vascular accidents. I. Role of cardiocirculatory insufficiency. *J.A.M.A.* 145:1227, 1951.
- ⁸⁵ Epstein, S. H.: Diabetic neuropathy and its prognosis. *Neurology*. 1:228, 1951.
- ⁸⁶ Woollong, K. R. and Rushton, J. G.: Serum neuritis. *Arch. Neurol. & Psychiat.* 64:568, 1950.
- ⁸⁷ Halpern, L.: A sensory pattern in radicular sciatica. *J. Nerv. & Ment. Dis.* 114:221, 1951.
- ⁸⁸ Menof, P.: New treatment for polyneuritis. *South African M. J.* 24:715, 1950.
- ⁸⁹ —: Role of vitamin B12 in polyneuritis, fatty degeneration and pernicious anemia. *South African M. J.* 25:394, 1951.
- ⁹⁰ Thiele, W. and Palm, S.: Intraspinal injection of toxoid in treatment of post-diphtheritic paralysis. *Med. Klin.* 45:84, 1950.
- ⁹¹ Nielsen, J. M.: Use of BAL in neurology. *Bull. Los Angeles Neurol. Soc.* 15:43, 1950.
- ⁹² —: Treatment of neuronitis with BAL. *Bull. Los Angeles Neurol. Soc.* 15:61, 1950.
- ⁹³ Sagana, J. S. and deOlaite, J. S.: Conservative treatment of trigeminal neuralgia. *An. méd. y cir. Barcelona*. 25:391, 1949.
- ⁹⁴ Davis, C. H., Jr. and Kunkle, E. C.: Benign essential (heredofamilial) tremor. *Arch. Int. Med.* 87:808, 1951.
- ⁹⁵ Steinche, K.: Peragit (artane) in treatment of Parkinsonism and other diseases. *Nord. med.* 45:919, 1951.
- ⁹⁶ Blumberg, A. G. and Dattner, B.: Benadryl and theophorin in the treatment of advanced Parkinsonism. *J. Nerv. & Ment. Dis.* 112:161, 1950.
- ⁹⁷ Dalsgaard-Nielsen, T.: Treatment of paralysis agitans with benadryl. *Nord. med.* 44:1526, 1950.
- ⁹⁸ Cumings, J. N.: The effects of BAL in hepatolenticular degeneration. *Brain*. 74:10, 1951.
- ⁹⁹ Yaskin, J. C.: Treatment of Parkinson's syndrome: some practical considerations. *Pennsylvania M. J.* 54:1156, 1951.

- ^{99a} Mjönes, Henry: Paralysis agitans. *Acta psychiat. et neurol.* 54: 1949.
- ¹⁰⁰ Hofer, E. Meyer: Insulin therapy in chorea minor. *Ann. Pædiat.* 176:297, 1951.
- ¹⁰¹ Chiavacci, L. V., Hoff, H., and Polvan, N.: Frequency of multiple sclerosis in Greater New York. *Arch. Neurol. & Psychiat.* 64:546, 1950.
- ¹⁰² Pratt, R. T. C., Compton, N. C., and McAlpine, D.: The familial incidence of disseminated sclerosis and its significance. *Brain.* 74:191, 1951.
- ¹⁰³ Spicknall, C. G., Kurland, L. T. et al.: Relation of brucellosis and multiple sclerosis. *J.A.M.A.* 143:1470, 1950.
- ¹⁰⁴ Eisele, C. W., McCullough, N. B., and Beal, G. A.: Brucellosis and multiple sclerosis. *J.A.M.A.* 143:1473, 1950.
- ¹⁰⁵ Campbell, A. M. G., Herdan, G., Tatlow, W. F. T., and Whittle, E. G.: Lead in relation to multiple sclerosis. *Brain.* 73:52, 1950.
- ¹⁰⁶ Gurthrie, T. C.: Visual and motor changes in patients with multiple sclerosis. *Arch. Neurol. & Psychiat.* 65:437, 1951.
- ¹⁰⁷ Yaskin, J. C., Spaeth, E. B., and Vernlund, R. J.: Ocular manifestations of 100 consecutive cases of multiple sclerosis. *Am. J. Ophth.* 34:687, 1951.
- ¹⁰⁸ Allison, R. S.: Survival in multiple sclerosis. *Brain.* 73:103, 1950.
- ¹⁰⁹ Weire, H. and Schrader, A.: Evaluation of cerebrospinal fluid in 300 cases of multiple sclerosis. *Ztschr. klin. med.* 145:576, 1949.
- ¹¹⁰ Muller, R.: Course and prognosis of disseminated sclerosis in relation to age of onset. *Arch. Neurol. & Psychiat.* 66:561, 1951.
- ¹¹¹ MacLean, A. R. and Berkson, J.: Mortality and disability in multiple sclerosis. *J.A.M.A.* 146:1367, 1951.
- ¹¹² Jonez, J. D.: Multiple sclerosis and allergy management with histamine therapy. *Ann. Allergy.* 8:44, 1950.
- ¹¹³ Aird, R. B.: Succinate therapy in multiple sclerosis. *Neurology.* 1:219, 1951.
- ¹¹⁴ Arkin, H., Sherman, I. C., and Weinberg, S. L.: Tetraethylammonium chloride in the treatment of multiple sclerosis. *Arch. Neurol. & Psychiat.* 64:536, 1950.
- ¹¹⁵ Strully, K. J., Gross, S. W., Schwartzman, J., and von Storch, T. C.: Progressive spinal cord disease. *J.A.M.A.* 146:10, 1951.
- ¹¹⁶ Bickerstaff, E. R.: Hereditary spastic paraplegia. *J. Neurol., Neurosurg. & Psychiat.* 13:134, 1950.
- ¹¹⁷ Barrett, E.: Spastic spinal paralysis responding to potassium therapy. *J.A.M.A.* 145:138, 1951.
- ¹¹⁸ Garland, H. G. and Artley, C. E.: Hereditary spastic paraplegia with amyotrophy and pes cavus. *J. Neurol., Neurosurg. & Psychiat.* 13:130, 1950.
- ¹¹⁹ Bunting, J. J.: Diabetic dorsal sclerosis of the spinal cord. *Dis. Nerv. System.* 12:245, 1951.
- ¹²⁰ Tom, M. I. and Richardson, J. C.: Hypoglycaemia from islet cell tumor of pancreas with amyotrophy and cerebrospinal nerve cell changes. *J. Neuropath. & Exper. Neurol.* 10:57, 1951.
- ¹²¹ Van Itallie, T. B. and Graves, S., Jr.: The use of priscoline in amyotrophic lateral sclerosis. *J. Nerv. & Ment. Dis.* 114:231, 1951.
- ¹²² Rabinovitch, R., Gibson, W. C., and McEachern, D.: Neuromuscular disorders amenable to wheat germ oil therapy. *J. Neurol., Neurosurg. & Psychiat.* 14:95, 1951.
- ¹²³ DeWind, L. T. and Jones, R. J.: Cardiovascular observations in dystrophia myotonica. *J.A.M.A.* 144:299, 1950.
- ¹²⁴ Kiloh, L. G. and Nevin, S.: Progressive dystrophy of the external ocular muscles (ocular myopathy). *Brain.* 74:115, 1951.

- ¹²⁵ Hammes, E. M., Jr. Periodic paralysis, *J.A.M.A.* 146:1401, 1951.
- ¹²⁶ Geddes, A. K. and Kidd, H. M.: Myasthenia gravis of the newborn. *Canadian M. A. J.* 64:152, 1951.
- ¹²⁷ McKeever, G. E.: Myasthenia gravis in a mother and her newborn son. *J.A.M.A.* 147:320, 1951.
- ¹²⁸ Perry, S. M.: Diabetes mellitus in association with myasthenia gravis. *J.A.M.A.* 143:1332, 1950.
- ¹²⁹ Thibaudeau, R.: Myasthenia gravis in a child aged four and a half years. *Laval méd.* 15:44, 1950.
- ¹³⁰ Torda, C. and Wolff, H. G.: Effects of administration of the adrenocorticothormone (ACTH) on patients with myasthenia gravis. *Arch. Neurol. & Psychiat.* 66:163, Aug. 1951.
- ¹³¹ Millikan, C. H. and Eaton, L. M.: Clinical evaluation of ACTH and cortisone in myasthenia gravis. *Neurol.* 1:145, 1951.
- ¹³² Rider, J. A. and Schulman, S.: Treatment of myasthenia gravis with octamethyl pyrophosphoramide. *J.A.M.A.* 145:967, 1951.
- ¹³³ Atkinson, W. J., Jr.: Treatment of myasthenia gravis tetraethyl pyrophosphate. *South. M. J.* 43:865, 1950.
- ¹³⁴ Patrikons, J. S.: Ophthalmoplegic migraine. *Arch. Neurol. & Psychiat.* 63:902, 1950.
- ¹³⁵ Fuchs, M. and Blumenthal, L. S.: Use of ergot preparations in migraine. *J.A.M.A.* 143:1462, 1950.
- ¹³⁶ Brentan, E.: Treatment of migraine with dramamine. *Rocky Mountain M. J.* 47:197, 1950.
- ¹³⁷ Gans, M.: Treating migraine by "sleep rationing". *J. Nerv. & Ment. Dis.* 113:405, 1951.
- ¹³⁸ Brain, W. R., Daniel, P. M., Greenfield, J. G.: Subacute cortical cerebellar degeneration and its relation to carcinoma. *J. Neurol., Neurosurg. & Psychiat.* 14:59, 1951.
- ^{138a} Hallgren, Bertil: Specific dyslexia. *Acta psychiat. et neurol.* 65: 1950.
- ¹³⁹ Gay, L. N.: Prophylactic and therapeutic control of vestibular disturbances with dimenhydrinate. *J.A.M.A.* 145:712, 1951.
- ¹⁴⁰ Slepian, A. and Hornby, W. B.: Neurologic complications associated with hereditary deforming chondrodysplasia. *J. Neurosurg.* 8:529, 1951.
- ¹⁴¹ Stone, T. T.: Peripheral facial palsy. *J.A.M.A.* 143:1154, 1950.
- ¹⁴² Kennedy, F., Efron, A. S., and Perry, G.: Grave spinal cord paralysis caused by spinal anesthesia. *Surg., Gynec. & Obst.* 91:385, 1950.
- ¹⁴³ Jewsbury, E. C. O.: Insensitivity to pain. *Brain.* 74:336, 1951.
- ¹⁴⁴ Martin, J. P.: Fits of laughter (sham mirth) in organic cerebral disease. *Brain.* 73:453, 1950.
- ¹⁴⁵ Johnson, D. R. and Chalgren, W. S.: Polycythemia vera and the nervous system. *Neurology.* 1:53, 1951.
- ¹⁴⁶ Ethelberg, S.: Symptomatic "cataplexy" or chalaistic fits in cortical lesions of the frontal lobe. *Brain.* 73:499, 1950.
- ¹⁴⁷ deMoragas, J.: Neurological sequelae of Rh factor. *Rev. clin. Españ.* 39:116, 1950.
- ¹⁴⁸ Frantz, C. H.: Orally given mephenesin in cerebral palsy. *J. A. M. A.* 143:424, 1950.
- ¹⁴⁹ Shy, G. M., Brendler, S. et al.: Effects of cortisone in certain neuromuscular disorders. *J.A.M.A.* 144:1353, 1950.

- ¹⁵⁰ Jonsson, B. and Von Reis, G.: Experience of ACTH and cortisone treatment in some organic neurological cases. *Acta. psychiat. et neurol.* 74:60, 1951.
- ¹⁵¹ Rothendler, H. H.: Bell's palsy treated with cortisone. *J. Nerv. & Ment. Dis.* 114:346, 1951.
- ¹⁵² Shy, G. M. and McEachern, D.: Further studies of the effects of cortisone and ACTH on neurological disorders. *Brain.* 74:351, 1951.
- ¹⁵³ —: The clinical features and response to cortisone of menopausal muscular dystrophy. *J. Neurol., Neurosurg. & Psychiat.* 14:101, 1951.

Otoneurology

By H. B. PERLMAN, M.D. AND J. R. LINDSAY, M.D.

AUDITORY SYSTEM

Clinical Observations

I^{VSTAM}¹⁷ sent questionnaires to the parents of over 400 children with deaf mutism in Sweden with respect to the role of rubella in the mother. He indicated that a wide variation in the incidence of deafness following rubella is reported from different countries.

He found that 31 mothers (12 per cent) of 261 children with deaf mutism of doubtful origin had had rubella within the first four months of pregnancy. A higher incidence of deaf mutism appeared during periods when rubella was unusually prevalent. Three to five per cent of the children of mothers who had had rubella during early pregnancy became deaf, while 10 to 20 per cent developed other malformations. The incidence appears high enough to warrant the use of some prophylactic measures. To be considered are the deliberate infection of young girls with rubella or the use of convalescent serum or gamma globulin when a pregnant woman is exposed to infection. The incidence of malformations in children following maternal rubella in Sweden seems hardly high enough to warrant interruption of pregnancy.

Schall, Lurie and Kelemen³¹ examined the temporal bones of two fetuses removed because of rubella in the mother. The temporal bone sections showed hemorrhages in the external and inner ear. Blood was found in all scalae of the cochlea and there were scattered hemorrhages within and around the membranous semicircular canals. The authors point out that a bleeding tendency is present in rubella. The development of the organ of Corti, nerve trunk, spiral ganglion and nerve branches corresponded to the fetal age. Arrest in development of the cochlea due to vascular damage was considered as a possible explanation for the deafness observed in such cases.

Hood¹⁶ describes two types of auditory fatigue. One occurs during the period of stimulation (per-stimulatory fatigue) and the other immediately following (post-stimulatory fatigue). The latter becomes suddenly large when a critical intensity is reached (i.e., 95 db. at 2048) and increases with the stimulus intensity. The first effect is a manifestation of adaptation and appears as a reduction in loudness to a new steady state when balancing

with the opposite unexposed ear. The reduction reaches a maximum in about three minutes. For the stimuli used the recovery rate of loudness after stimulation is greatest in the first few seconds and is complete after a minute. In Ménière's disease after a preliminary loudness balance the loudness of a constant tone in the affected ear dropped in a few seconds to a new steady level, as measured by balancing at short intervals with the normal ear. According to the author this is an example of susceptibility to per-stimulating fatigue and may be related to disease of the end organ.

Eby and Williams⁸ carried out alternate binaural loudness balance tests on 16 patients with tumors in relation to the 8th nerve who had partial deafness. Recruitment was absent or only slight in these cases. Diplacusis was present in only one case. On the other hand, in 33 patients with presumed end organ damage (Ménière's), recruitment was present. Diplacusis was noted in twenty-three of these. Speech tests in cases with recruitment showed that intelligibility reached a maximum and then decreased with increase in intensity. It appeared that loudness recruitment and decreasing speech intelligibility were expressions of the same fundamental disorder. These findings support those previously reported by Dix, Hallpike, and Hood that recruitment is absent in disease of the auditory nerve.

By an acoustic balance method previously described, Metz²⁶ recorded the change in impedance of the drum during reflex acoustic contraction of the middle ear muscles in the normal human subject in response to an acoustic stimulus in the opposite ear. A latency of about 35 milliseconds was measured. This latency decreased with increasing intensity. The onset of the impedance change was abrupt; the termination much slower, and the effect lasted longer than the stimulus. The impedance increased with increasing intensity of the stimulus. The first recorded changes occurred to stimuli at about 80 db. above threshold.

Schuknecht, Neff, and Perlman³³ produced deafness in conditioned cats by blows on the head. A metal rod placed in the exposed skull was struck with a hammer. The resultant bone conducted shock pulse produced various degrees of damage to the organ of Corti with secondary ganglion and nerve fiber degeneration. Intracochlear hemorrhage was also produced. The greatest anatomic damage was associated with the greatest functional loss. The trauma centered around the upper end of the basal cord and a high tone deafness was most marked.

Stuart, O'Brien and McNally³⁴ point out that thrombosis of the cerebral veins with hemorrhagic softening and necrosis of the brain may follow infection of the paranasal sinuses and the middle ear. Sixteen cases of this type were studied. Palsies and focal seizures affecting the face, hand, fingers and arm were common. This complication is less frequent than that of brain abscess with which it may be confused. The occurrence of cerebro-

venous thrombosis in childhood as a complication of infection may be a cause for epilepsy, especially of the focal type.

Auditory System, Experimental

Many electrical studies on the auditory system in the experimental animal have appeared during the year. They greatly enlarge our understanding of the role of the various components in this system.

Van Eyck³⁷ observed the increased action potential in a pigeon with ankylosis of the columella, after fenestration of the semicircular canal. The sound was introduced in the external auditory canal. The anatomic relations in the pigeon are such that the stimulus could not reach the new fenestra. Only the round window could be the pathway to the cochlea. The new window consequently allows for the compensatory movements of the labyrinth fluid. This he believes indicates the mechanisms of response in the fenestrated ear in man.

This experiment gives further evidence that the cochlea may be stimulated by sound waves impinging on the round window but it does not prove that this is the mechanism of cochlear stimulation in the fenestrated human ear. The anatomic relations do not correspond.

Lowenstein and Roberts²⁴ continued their observations on the isolated elasmobranch labyrinth and extended them to the vibration receptors. They found that the anterior two-thirds of the saccular macula, the macula neglecta and part of the utricle (Lacinia) not covered by otolith gave vibration responses. Increased firing rate per fiber and an increased number of responding fibers probably resulted from the stimulation. A limitation of the response to vibrations below 120 cycles per second, may have been due to the experimental technic. Some synchronization between signal frequency and spike discharge rate in the nerve was observed and, according to the authors, may form a basis for pitch discrimination.

In addition to the well known alternating potential of the cochlear microphonic and the characteristic nerve action potential, Bekesy² discovered a constant potential difference between the scala tympani and scala vestibuli. A sudden change in this potential occurred with the onset of an acoustic stimulus. The behavior of this direct current potential in the cochlea to sudden movements of the cochlear partition and to anoxia indicates to Bekesy³ that the direct current in the cochlea is generated by continuous biochemical processes in the cochlear duct, and that the total cochlear microphonic is not just due to the transformation of the mechanical energy of the vibrating partition.

Bekesy⁴ also measured the electrical resistance along the cochlea and points out that the voltage drop resembles that in a transmission line. He found that the bony wall of the cochlea is a good insulator and that the

main grounding pathway of the electrical potential within the cochlea to the body is via the brain along the nerves and blood vessels in the internal meatus.

Bekesy⁴ produced microphonics by local mechanical movement of the basilar membrane with a vibrating electrode. He found that the microphonic was related to the amplitude of movement of the basilar membrane and not to the acceleration. On the other hand, the microphonic produced by vibrating Reissner's membrane was partly related to the velocity. This indicated that frictional forces are developed as the vibration of Reissner's membrane is transmitted to deeper parts of the cochlear duct. Vibration of the wall of the utricle also produced electrical responses.

Davis, Fernandez and McAuliffe⁷ describe a summation potential of the cochlea which behaves differently from the microphonics and the action potential. In response to tone pips, it appears as a direct current potential superimposed on the alternating potential of the microphonic that precedes the characteristic action potential. The authors think it originates in the organ of Corti and that it resembles the potential obtained at neuromuscular junctions and from pressure and touch receptors.

In cats, Krejci and Bornschein²¹ found a reversible reduction in the cochlear potential with increased intracranial pressure. They believe that this is due to circulatory changes in the labyrinth vessels secondary to the increased pressure and not to changes in the physical impedance of the labyrinth fluid system. They observed some of these changes in the vessels through the round window membrane.

These experimental findings in the cat are difficult to relate to clinical observations. There is strikingly little change in auditory function in patients with increased intracranial pressure.

Schuknecht and Neff³³ found low tone hearing loss in conditioned cats after needle lesions in the apical turns of the cochlea.

There is further work on streptomycin poisoning. Ruedi³⁰ reports that loss of vestibular and cochlear function results in guinea pigs given 30 gm. of streptomycin in 160 days, and finds histologic changes in the sensory epithelium of the cochlea and vestibular end organs. The organ of Corti is affected and in one case he found it gone symmetrically on both sides for the entire first turn of the cochlea with ascending degeneration of the afferent fibers of the spiral ganglion, the ganglion cells and the nerve trunk. Changes in the *stria vascularis* through this area were also observed. The minor changes seen in the central cochlear and vestibular nuclei were thought by Ruedi to be non-specific. He found similar end organ changes in patients who died of tuberculous meningitis who had received streptomycin and had become totally deaf. On the other hand, Hertz, Riskaer

and Vraa-Jensen¹⁵ find no signs of damage to the sensory cells in the labyrinth of guinea pigs after abolishing cochlear and vestibular function with 400 mg. of streptomycin per kilo for three or four weeks. However, alterations of the central cochlear and vestibular nuclei were found. They previously reported that in such animals the cochlear microphonic responses were normal. Glorig¹² found that in addition to vestibular losses dihydrostreptomycin produced nerve deafness in about 25 per cent of patients receiving 2 to 3 grams per day for 3 months or more. Usually this loss did not appear before 3 months but the loss might progress even after discontinuing the drug. Once a significant hearing loss developed the process was irreversible. He prefers the use of streptomycin for prolonged therapy as in tuberculosis.

Exploring the responses of the cochlear nucleus in the cat with microelectrodes, Galambos, Rose, and Hughes¹¹ found in response to threshold stimuli, a characteristic frequency response dropping from high to low as the electrode moves down from above in the frontal plane. Single units with a wide range of characteristic frequencies were also found. Thurlow et al¹³ explored the inferior colliculus with microelectrodes. The maximum rate of acoustic stimulation (clicks or sine waves) which gave a response was about 400 per second. The discharge rate of the evoked action potential spike increased up to a maximum of 100 per second with the intensity of the stimulus. Continuous acoustic stimulation caused a progressive reduction in the discharge rate from the inferior colliculus to complete absence after a few seconds of stimulation.

Lennox and Madsen²² report that at the collicular level in a decerebrate cat electrical responses varied widely with respect to form, amplitude and duration with variation in the frequency of a pure tone stimulus while variation in the intensity of the stimulus did not produce all these variables. They believe that different frequencies may, therefore, have different rates of transmission and this may be a factor in sensory discrimination.

The medial geniculate body in the cat was explored with microelectrodes by Gross and Thurlow.¹⁴ Some frequency distribution was found. The spike potential did not change in magnitude with change in intensity of the stimulus but did change in frequency up to about 100 spikes per second. Adaptation to sustained stimuli was complete in about 5 seconds.

At the cortical level, Rosenzweig²⁹ found that in the cat both ears are represented with overlapping in each auditory cortex and that the response on one side to clicks was larger from the contralateral than the ipsilateral ear. When a click was delivered in rapid succession to each ear, the amplitude of the second response was reduced. He suggests that discrimination at the cortex to differences in time of arrival of the acoustic stimulus at the two ears may be related to the ability to localize the source of sound.

Rosenblith and Rosenzweig²⁸ report that the cortical response to supra-threshold clicks delivered to one ear is essentially unaffected after the opposite ear is exposed to loud sounds.

Continuing his investigation of the response of small strychninized patches of the middle ectosylvian area in the dog, Tunturi³⁶ reports that both ears use the same frequency elements in each cortex but that greater intensity is needed when stimulating the ipsilateral ear. For the upper frequencies this difference was least, and grew to 40 to 80 db. for the lower frequencies. This indicates that there is an intensity representation in the cortex for the ipsilateral ear. The intensity gradient is about .2 mm. per db. The character of the electrical discharge in the cortex is not changed by changes in frequency or intensity of the stimulus. Only presence or absence of discharge in an area of the cortex is signalled. Therefore, information regarding the frequency and intensity of tones appears to be related only to the position of the elements in the area. These two stages of activity of the cortical elements can be indicated as 1 and 0, the digits of a binary system of numbers. Since the smallest measured elements in the middle ectosylvian are .2 mm. or .1 octave in the frequency dimension, about 70 such cortical elements would be present between 100–12,000 cps. Thus, 10^{26th} or 2^{70th} pieces of information with respect to frequency can be represented in the area.

Chow⁵ counted the nerve cells at various centers in the auditory system of two monkeys and found that there were about 88,000 in the cochlear nucleus, 34,300 in the superior olivary complex, 38,100 in the nucleus of the lateral lemniscus, 392,000 in the inferior colliculus, 364,000 in the parvocellular area of the medial geniculate, 58,000 in the magnocellular division and 10,200,000 in the auditory cortex. For every .002 mm.³ the cochlear nucleus contained 31 cells, the superior olivary complex 29 cells, the inferior colliculus 84 cells, the parvocellular part of the medial geniculate 65 cells, the magnocellular part 38 cells, and the auditory cortex 186 cells. Thus, the number of neurones increase in successive steps from the spiral ganglion to the auditory cortex. Already in the cochlear nucleus there are about three times as many neurones as in the spiral ganglion. In the auditory cortex there are at least eight times as many neurones as in medial geniculate. The author points out that any theory of auditory function must take these observations into account.

Penfield and Rasmussen²⁷ summarized their observations on the subjective sensations produced by electrical stimulation of the cortex in man. The area found to be active was close to the fissure of Sylvius. In most cases, a 60 cycle stimulus was used. In the majority of cases stimulation failed to produce any auditory response. When sounds were sensed it was usually referred to the contralateral ear, sometimes to both ears. A high

pitched continuous tone like the noise of a cricket, bell or whistle, an interrupted tone like the chirping of birds, a rushing sound like the wind through the trees, or the hum of a motor were described. In one case where the auditory sensory area within the fissure of Sylvius was accessible, stimulation produced ringing in both ears. Occasional mild dizziness (swaying, turning, falling) was produced from stimulation of this area.

Licklider²³ proposed a duplex theory of pitch perception. He suggests that in addition to a frequency separation of the stimulus along the cochlear duct, the central nervous system carries out an autocorrelation analysis of the time relations of the train of nerve impulses into which the cochlea transforms the stimulus. For this theory the input to the nervous system must be divided near the cochlea into two channels, one with and one without a built-in delay system. The author refers to the findings of Lorente de N  that the first auditory fibers branch into two divisions, one taking a one synapse route to the next relay station, the other passing into a region of dense ramifications and synaptic connections.

VESTIBULAR SYSTEM

Clinical and Experimental Observations. Jongkees¹⁸ studied the function of the labyrinth in a patient with part of the membranous horizontal canal accidentally torn away during a fenestration operation. Despite the injury an improvement of hearing was obtained. At first, no caloric reaction was obtained, then a persistent asymmetry between the hot and cold caloric test was noted and no change in the direction of caloric nystagmus with changes in position of the head. A preponderance of the opposite side was present even after two years. The author points out that both hot and cold caloric tests are needed to recognize a normal vestibular reaction.

Jongkees and Hulk¹⁹ studied, by cupulometry, the vestibular function of 30 bed patients with no hearing impairment who received 1.2 grams of streptomycin daily for pulmonary tuberculosis. They found that the sensation of rotation was not directly related to the nystagmus. The first changes in sensation appeared after changes in nystagmus were seen. Increased nystagmus thresholds up to total disappearance, or gradual reduction in the amplitude of nystagmus without change in threshold were found. The threshold of sensation of rotation became higher, but even when nystagmus could not be elicited, sensation of rotation might still be good. Nystagmus after rotation failed to appear about the same time that the caloric test disappeared. Until then the duration of the caloric test remained unchanged. A partial or complete recovery within two months following cessation of therapy was found in 50 per cent of the cases with absent function.

Fernim, Deinse and Hammelburg¹⁰ were able to abolish temporarily the labyrinth reflexes in a rabbit with dramamine and observed the order in

which these recovered. They found that the semicircular canal reflexes returned first and the otolith reflexes last. They reasoned from this that dramamine had more effect on the otolith reflexes and that this was related to the effect of this drug in motion sickness. They encourage its use in Ménière's disease.

Ersner, Spiegel and Alexander⁹ report on the treatment of Ménière's disease by the transtympanic injection of 2 per cent cocaine or 35 to 50 per cent alcohol. After twenty minutes, the patient develops vertigo, deafness and nystagmus to the opposite side that may last a few hours. In addition to the prevailing hearing loss, the hearing drops 30 to 40 db. Vertigo completely subsided in eleven and was improved in nine out of 37 unilateral cases treated. Facial paralysis did not occur in any of the patients.

Altmann and Montreuil,¹ from observations in man and in the monkey, recommended that when coagulation of the labyrinth is indicated for Ménière's disease a strong current should be used to produce adequate vestibular damage. Experimentally, they also found that a circumscribed fibrosis around an obstructing bone chip effectively plugs the membranous semicircular canal. This was, thus, carried out in three cases of Ménière's disease. In two, the dizzy attacks were practically stopped and some of the hearing was retained. In the third, hearing was completely lost and the attacks of dizziness continued unabated.

In the dark, a subject exposed to a centrifugal force, feels he is tilted and an illuminated line appears to rotate. The amount and direction of apparent tilt of the body and visual field is related to the resultant of the force of gravity and the centrifugal force. The illusion is apparently due to stimulation of the otoliths. (See previous reports by Graybiel.) Graybiel and Brown¹³ now report on the time lag between the fully developed visual disorientation and the fully developed centrifugal force. For the forces used, a mean time delay of 81 seconds was measured. They point out that this delay may be related to the nature of otolith movement or to the time required at the cortical level for proper integration of incoming impulses. This time lag is important to aviation since the full disorienting effect of a centrifugal force will not become manifest if the exposure time is short.

A patient with partial 8th nerve paralysis following streptomycin therapy for tuberculous meningitis was tested by Mann²⁵ for space perception. The caloric response was absent and there was partial deafness worse in the left ear. In the absence of visual clues, the patient seated in a chair, was tilted. Then he was asked to return the chair to the vertical position. He made greater than normal errors. Unlike the normal, the error did not increase when the tilted position was maintained for sixty seconds. From a tilted position, there was difficulty in adjusting a narrow luminous line to the gravitational vertical. Intra and post-rotatory illusions of movement

and nystagmus were also reduced. Cranmer⁶ produced nystagmus to the same side by stimulating with a needle electrode the lateral and medial vestibular nuclei in the anesthetized monkey. A destructive lesion produced nystagmus to the opposite side. Stimulation of the superior vestibular nucleus produced vertical nystagmus. Deep anesthesia abolished both the slow and quick components of the nystagmus. Nystagmus from lesions of the cerebellar pyramis and nucleus fastigii was also observed. After destruction of the right lateral vestibular nucleus, rotation of the animal to the right did not produce normal deviation of the eyes to the left. Nystagmus to the right was absent after rotation to the left. After destruction, nerve fiber degeneration was followed from the destroyed lateral vestibular nucleus to the abducens nucleus. There was no degeneration in the medial longitudinal fasciculus above the abducens nucleus.

The cortical projection of the vestibular system was studied in the cat by Kempinsky.²⁰ Stimulating the fibers of the 8th nerve after previous ablation of the cochlea and facial nerve, surface positive waves of about 100 microvolts were evoked having a 10 to 12 millisecond latency. The center of these responses was in the anterior descending limb of the suprasylvian gyrus, between the anterior margin of the auditory receiving area and the posterior margin of the arm and face tactile receiving area. The author admits, however, that a projection from the nervous intermedius to this cortical region could not be excluded.

REFERENCES

- ¹ Altmann, F. and Montreuil, F.: The surgical treatment of Ménière's disease: experimental and clinical investigations. *Ann. Otol., Rhin., & Laryng.* 70:308-326, 1951.
- ² Bekesy, G. V.: Direct current potentials and energy balance of the cochlear partition. *J. Acoust. Soc. America.* 23:576-582, 1951.
- ³ —: The coarse pattern of the electrical resistance in the cochlea of the guinea pig (electro-anatomy of the cochlea). *J. Acoust. Soc. America.* 23:18-28, 1951.
- ⁴ —: Microphonics produced by touching the cochlear partition with a vibrating electrode. *J. Acoust. Soc. America.* 23:29-35, 1951.
- ⁵ Chow, K. L.: Numerical estimates of the auditory central nervous system of the rhesus monkey. *J. Comp. Neurol.* 95:159-175, 1951.
- ⁶ Cranmer, R.: Nystagmus as related to lesions of the central vestibular apparatus and the cerebellum. *Ann. Otol., Rhin., & Laryng.* 60:186-197, 1951.
- ⁷ Davis, H., Fernandez, C., and McAuliffe, D. R.: Theory of audition. Process of electrical excitation of the ear. *Ann. d. Telecommun.* 6:197-201, 1951.
- ⁸ Eby, L. F. and Williams, H. J.: Recruitment of loudness in the differential diagnosis of end organ nerve fiber deafness. *Tr. Am. Laryng., Rhin., & Otol. Soc.* 134-148, 1951.
- ⁹ Ersner, M. S., Spiegel, E. A., and Alexander, M. H.: Transtympanic injection of anesthetics for the treatment of Ménière's syndrome. *Arch. Otolaryng.* 54:43-52, 1951.

- ¹⁰ Fernim, H., Van Deinsse, J. V., and Hammelburg, E.: The effect of dimenhydrinate upon the labyrinth. *Acta oto-laryng.* 38:543-549, 1951.
- ¹¹ Galambos, R., Rose, J. E., and Hughes, J. R.: Frequency localization in cochlear nucleus. *Proc. Am. Physiol. Soc.* 10:47, 1951.
- ¹² Glorig, A.: The effect of dihydrostreptomycin hydrochloride and sulfate on the auditory mechanism. *Ann. Otol., Rhin. & Laryng.* 60:327-335, 1951.
- ¹³ Graybiel, A. and Brown, R. H.: The delay in visual reorientation following exposure to a change in direction of resultant force on a human centrifuge. *J. Gen. Psychol.* 45:143-150, 1951.
- ¹⁴ Gross, N. B. and Thurlow, W. R.: Microelectrode studies of neural auditory activity of cat; no. 2., medial geniculate body. *J. Neurophysiol.* 14:409-422, 1951.
- ¹⁵ Hertz, H., Riskaer, N., and Vraa-Jensen, G.: Histological investigation in chronic streptomycin poisoning in guinea pigs. *Ann. Otol., Rhin. & Laryng.* 60:343-349, 1951.
- ¹⁶ Hood, J. D.: Studies in auditory fatigue and adaptation. *Acta oto-laryng. Suppl.* #92, 1951.
- ¹⁷ Ivstam, B.: Rubella and deaf mutism in Sweden. *Acta oto-laryng.* 39:380-387, 1951.
- ¹⁸ Jongkees, L. B. W.: On the function of the labyrinth after destruction of the horizontal canal. *Acta Oto-laryng.* 38:505-510, 1951.
- ¹⁹ — and Hulk, J.: The action of streptomycin in vestibular function. *Acta Oto-laryng.* 38:225-232, 1951.
- ²⁰ Kempinsky, W. H.: Cortical projection of vestibular and facial nerves in cat. *J. Neurophysiol.* 14:203-210, 1951.
- ²¹ Krejci, F. and Bornschein, H.: Animal experiments in cochlear function with changes of intracranial pressure. *Pract. oto-rhino-laryng.* 13:146-166, 1951.
- ²² Lennox, M. and Madsen, A.: The effect on acoustic responses of frequency, amplitude and pure tones. *EEG. & Clin. Neurophysiol.* 3:382, 1951.
- ²³ Licklider, J. C. R.: A duplex theory of pitch perception. *Experientia.* 7:128-134, 1951.
- ²⁴ Lowenstein, D. and Roberts, T. D. M.: The localization and analysis of the responses to vibration from the isolated elasmobranch labyrinth: a contribution to the problem of the evolution of hearing in vertebrates. *J. Physiol.* 114:471-489, 1951.
- ²⁵ Mann, C. W.: The effects of auditory and vestibular nerve pathology in space perception. U.S. Nav. School of Aviat. Med. Research Report #22. N.M. 001 065 01.22, Aug. 1951.
- ²⁶ Metz, O.: Studies on the contraction of the tympanic muscles as indicated by changes in the impedance of the ear. *Acta Oto-laryng.* 39:397-405, 1951.
- ²⁷ Penfield, W. and Rasmussen, T.: A clinical study of localization of function. *In The Cerebral Cortex of Man.* New York, The MacMillan Co., 1950, pp. 149-155.
- ²⁸ Rosenblith, W. A. and Rosenzweig, M. R.: Further electrophysiological observations on auditory masking and fatigue. *J. Acoust. Soc. America.* 23:633, 1951.
- ²⁹ Rosenzweig, M. R.: Representations of the two ears at the auditory cortex. *Am. J. Physiol.* 167:147-158, 1951.
- ³⁰ Ruedi, L.: Therapeutic and toxic effects of streptomycin in otology. *Laryngoscope.* 61:613-636, 1951.
- ³¹ Schall, L. A., Lurie, M. H., and Kelemen, G.: Embryonic hearing organs after maternal rubella. *Laryngoscope.* 61:99-112, 1951.

- ³² Schuknecht, H. F., Neff, W. D., and Perlman, H. B.: An experimental study of auditory damage following blows to the head. *Ann. Otol., Rhin. & Laryng.* 60: 273-289, 1951.
- ³³ Schuknecht, H. F. and Neff, W. D.: Hearing loss after experimental injury to the apex of the cochlea. *Proc. Am. Physiol. Soc.* 10:122, 1951.
- ³⁴ Stuart, E. A., O'Brien, F. H., and McNally, W. J.: Cerebral venous thrombosis. *Ann. Otol., Rhin. & Laryng.* 60:406-438, 1951.
- ³⁵ Thurlow, W. R., Gross, N. B., Kemp, L. H., and Lowy, K.: Microelectrode studies of neural auditory activity of cat; no. 1, inferior colliculus. *J. Neurophysiol.* 14:289-304, 1951.
- ³⁶ Tunturi, A. R.: A difference in the representation of the two ears in the isofrequency bands of the MES auditory area in the dog. *J. Acoust. Soc. America.* 23:635, 1951.
- ³⁷ Van Eyck, M.: The function of the round window in the transmission of the sound waves after fenestration of the labyrinth. *J. Laryng. & Otol.* 65:183-186, 1951.

Neurosyphilis

By BERNHARD DATNER, M.D. AND MARTIN A. GREEN, M.D.

IN HIS paper on juvenile and senile types of G. P. I., Stewart writes: "No one who is familiar with the vast literature devoted to Neurosyphilis can fail to be impressed by the infrequency with which general paresis of the insane now claims attention in current medical journals." Stewart believes that this is due to the rapid decline in admissions of paretics to mental institutions in England and Wales, where the rate of paretics in the hospital population fell from 7.4 per cent during the period 1908 to 1912 to 3.9 in 1937. Similar observations were reported from other European countries and in the United States of America. However, a review of the literature covering the years 1950 and 1951 reveals a greatly diminished number of papers dealing with general paresis and with neurosyphilis in general. Since in the last few years the influx of new cases of parenchymatous or meningovascular neurosyphilis is decreasing, the published material consists mostly of follow-up reports on patients treated in the past.

Nielsen has written a paper of considerable interest with regard to the incidence of neurosyphilis in patients with syphilis. The author attempted a follow-up of 467 patients admitted between 1913 and 1920 for early syphilis to the Rigs Hospital in Copenhagen. Almost all patients had received 1 to 3 Gm. of old Salvarsan in three to six injections and 50 or more mercury rubs. The re-examination was terminated in 1949 and the study, therefore, constitutes a follow-up of 29 to 36 years. Only 40 patients (8.6 per cent) developed neurosyphilis and of those 5 (1.1 per cent) developed tabes and 20 (4.3 per cent) developed general paresis. These figures correspond closely to those reported in the literature as to the incidence of neurosyphilis in patients with acquired syphilis without treatment. It must, therefore, be concluded that treatment as given at Rigs Hospital between 1913 and 1920 was inadequate. The highest rate of neurosyphilis was found in the group of 275 patients, with secondary syphilis. Of these, 15 developed meningovascular neurosyphilis, 5 tabes and 20 general paresis.

Willcox made a survey of 117 inmates of an African mental hospital who

had previously shown positive or doubtful evidence of syphilis. Abnormalities of the spinal fluid were found in 14 patients. In addition, there were between 18 and 22 other inmates with normal spinal fluids who were considered as possibly having undergone "cure," spontaneous or otherwise. Of these 117 patients, 78 were epileptics. No evidence was obtained that meningovascular syphilis was responsible for the bulk of African epilepsy. Another study undertaken by Willcox revealed that the results of serologic testing for syphilis of 658 patients in an African mental hospital did not show an appreciably higher incidence of positive reactions than were obtained in a general population; altogether 32 to 36 cases of neurosyphilis were discovered. Willcox confirms that neurosyphilis in the African manifests itself in its meningovascular or vascular forms rather than as paresis or tabes.

The controversy about the relative value of penicillin alone or penicillin plus fever or penicillin plus arsenicals and heavy metals is still going on, but judging from the recent conversion of some of the outstanding advocates of the combined treatment methods it seems quite obvious that penicillin alone will be the treatment of choice for all types of neurosyphilis very soon. Strong support for this belief is given by a joint declaration of a distinguished group of members of the American Academy of Dermatology (Curtis, Kitchen, O'Leary, Rattner, Rein, Schoch and Shaffer) who informed the medical profession through the Journal of the American Medical Association, that a course of 6 to 12 million units of penicillin is usually adequate "as an effective method of treating neurosyphilis of all types." This is the more remarkable as O'Leary previously (vide review of 1950) did not believe in the effectiveness of penicillin alone and Curtis originally had grave doubts about penicillin as the sole therapeutic agent in general paresis and tabetic optic atrophy.

Whenever penicillin is combined with fever therapy, malaria inoculation or electropyrrexia is being used. Only Noojin and co-workers report on typhoid vaccine as fever producing agent. By giving intravenous injections of typhoid vaccine twice or three times daily the authors were able to produce prolonged elevation of temperature without abnormal risks or excessive expense.

One of the arguments for the supposed ineffectiveness of penicillin in neurosyphilis was the observation that penicillin injected intramuscularly does not penetrate into the spinal fluid. Wright, Thayer, Nicholson and Arnold studied 114 patients of whom 70 had negative spinal fluids. Every patient received 600,000 units of procaine penicillin every 24 hours for six doses. Two hours after the first injection a trace of penicillin was found in 9 per cent of 11 specimens and 9 per cent showed a quantitative level. Between 31 hours and 194 hours, penicillin was detected in 75 per cent of

110 specimens. The authors conclude that penicillin can be demonstrated in the spinal fluid of a large percentage of patients following one to six intramuscular injections of moderate amounts of microcrystal procaine penicillin in oil.

Smith studied 18 patients with parenchymatous neurosyphilis. When small doses of penicillin were given, detectable amounts appeared in the serum but not in the spinal fluid. When, however, large doses were given, large amounts of penicillin were found in the spinal fluid. From the results of this investigation a scheme of dosage for the treatment of neurosyphilis is suggested. Penicillin is given every three hours on the first day, 20,000 units for eight doses, on the second day 50,000 units for eight doses, on the third day 100,000 units for eight doses and from the 4th to 10th day 500,000 units every four hours for 42 days—a total of more than 20 million. During the past two years 20 patients have been treated with this dosage without a Herxheimer reaction, signs of any meningeal irritation or convulsions. One will object to such an elaborate schedule of treatment when experience has shown that daily injections of PAM (penicillin in oil with aluminum monostearate) give highly satisfactory results without provoking serious reactions. In addition, it is more important that a proper concentration of penicillin is obtained in the tissues of the central nervous system, which harbor the spirochetes, than in the spinal fluid. For the same reason, there is no need for intrathecal injections of penicillin, which, as has been repeatedly reported, are not without danger. Moragues and Wyatt lost a 50-year-old female patient who, following a second intrathecal administration of penicillin, developed a sudden onset of hemoglobinemia and hemoglobinuria and died in shock.

Mild Herxheimer reactions have been repeatedly encountered in the treatment of neurosyphilis. They may consist of an aggravation of mental symptoms in paretics, occasionally a patient with so-called asymptomatic neurosyphilis may become manifestly psychotic. Putkonen and Rehtijärvi studied 229 patients with neurosyphilis by administering an initial dose of at least 100,000 units of penicillin and recording the temperature of the patient at hourly intervals. They found a febrile reaction in all 22 patients with dementia paralytica who had no previous treatment. Patients with asymptomatic neurosyphilis showed this febrile reaction in only 12 per cent, patients with meningovascular syphilis in 16 per cent and those with tabes in 9 per cent. Increased abnormality of the cerebrospinal fluid caused an increase in the incidence of febrile responses. When the spinal fluid was of grade III, 40 per cent of the patients showed a reaction, whereas those of grade II included only 5 per cent reactions. The minimal elevation of temperature occurred a few hours later in neurosyphilis than in primary or secondary syphilis, mostly 12 to 16 hours after injection of penicillin. The

authors attribute this delayed reaction to the fact that penicillin penetrates into the perivascular foci of spirochetes of early syphilis more rapidly than into those present within the brain.

More serious were the reactions observed by Shapiro and Berris. The authors treated 10 patients with neurosyphilis and one patient with tertiary syphilis of the skin with gradually increasing doses of crystalline penicillin G starting with as little as 5000 units every three hours. After the fifth day, daily injections of one million units dissolved in 500 cc. of normal saline were given intravenously (!) in 60 minutes. Of the 11 syphilitic patients so treated, 8 had toxic reactions and 2 of them subsequently died. All patients, including 3 of 6 non-syphilitic control patients, complained of malaise, headache, nausea, chilly sensation and elevation of temperature. In all but one case the reaction occurred one to three hours after the termination of the intravenous infusion of penicillin. The authors feel that this report "serves to underwrite the need for caution in the use of this drug in the treatment of central nervous system syphilis." The authors suspect that the reactions may have been due to sensitization by the preceding intramuscular doses of penicillin or to a direct neurotoxic action of penicillin, but do not seem aware of the known danger of its intravenous application. Their warning, therefore, should be directed against their method of using penicillin rather than against the use of the most valuable therapeutic agent in the management of neurosyphilis.

A Herxheimer reaction occurred in a patient of Bush despite initiation of penicillin therapy in small doses. The patient, a colored male, age 38, had had three epileptiform seizures prior to admission. No antisyphilitic treatment was given during the preceding six years. Treatment was started with 5000 units of crystalline penicillin in aqueous solution every three hours for eight doses and then 10,000 units every three hours. At 30 and 60 hours after the first penicillin injection the patient experienced a grand mal. After the second seizure he developed acoustic and visual hallucinations and, therefore, treatment was discontinued. But three days later a prolonged grand mal seizure occurred, the temperature rose to 104, coma set in, the patient went downhill and died 24 hours later. At autopsy, a syphilitic meningoencephalitis with hemorrhages into the white matter of the frontal and temporal lobes bilaterally was found. From this observation the author concludes that a Herxheimer reaction is an "all or none" reaction, which may be set off in full intensity by very small initial doses of penicillin and he advocates, therefore, a preliminary course of bismuth prior to penicillin therapy. One wonders whether these deductions are justifiable in view of the extreme rarity of such reactions. At Bellevue, where more than 600 patients with neurosyphilis have been treated in the past eight years, not one case of a fatal Herxheimer reaction has been observed although all the patients

were started originally with at least 20 or 30,000 units penicillin in aqueous solutions and later on with 600,000 units of procaine penicillin in oil as the first dose. The fact that the patient had "epileptiform" seizures at the time of admission may indicate that he belonged to the unfortunate group of the so-called galloping type of general paresis. This is the most dangerous form of paresis and could not be arrested by any of the formerly used therapeutic methods. In recent years, however, we have seen quite a few of these patients saved by rather *large* doses of penicillin, i.e., intramuscular injections of 300,000 or 600,000 units every four hours for 10 to 15 days. Bismuth has never proved effective in the treatment of parenchymatous neurosyphilis and would, therefore, probably be of little help.

As previously mentioned, most of the recent papers on neurosyphilis deal with the relative effectiveness of penicillin alone versus penicillin plus fever.

Ford and co-workers treated 112 patients with asymptomatic neurosyphilis with penicillin alone. All patients were treated with no less than 4.8 million units penicillin in not less than eight days. Of these 112 patients, 102 showed an inactive spinal fluid and only 10 patients (8.9 per cent) either failed to attain a normal cell count within six months, or showed an initial favorable response followed by a secondary rise later on. One patient failed to respond to two courses of aqueous penicillin and one to nine million units of aqueous penicillin. Most failures occurred during the first year of post-treatment observation. With a dosage of not less than five million units, preferably nine million units in ten days, the authors find penicillin superior to any other form of treatment in asymptomatic neurosyphilis.

Whether or not the laboratory findings are of greater significance than the clinical status in the follow-up of treated patients is discussed by Packer. He sides with Dattner and Thomas and finds the concept of the activity of the syphilitic process as mirrored in the spinal fluid findings "an important contribution in that it provides the physician with objective laboratory tests, well within the reach of the office laboratory, as criteria for guidance in therapy. . . . On the basis of our experience with the treatment of over 500 cases of neurosyphilis at the Gailor Psychiatric Hospital in Memphis, it is our feeling that this concept has proved to be a reliable guide in the therapy of syphilis." Packer comes out strongly in favor of penicillin alone. The author admits that fever therapy "wrought many miraculous recoveries, and was beyond question the treatment of choice for late neurosyphilis before penicillin appeared on the scene. However, mortality rates of from 5 to 20 per cent were associated with its use in general paresis, and the ordeal for the patient and for the physician alike was a great one. The hazard from penicillin therapy is practically nil."

In an international symposium on the study of syphilis, given in September-October, 1950 in Helsinki and Paris, Dattner discussed the diagnostic and therapeutic problems in neurosyphilis. He emphasized that no syphilologist is able to deal with his patients successfully without a proper understanding and evaluation of the spinal fluid syndromes. Much confusion about the best methods of treatment could be cleared and occasionally much harm to the patients could be prevented if physicians dealing with neurosyphilis were aware of the fact that clinical signs and symptoms are by no means reliable guides to the effectiveness of therapy, and that further attempts to kill spirochetes are useless when the infection has already been arrested or cured. In another paper, Dattner, Thomas and de Mello point out that after treatment of neurosyphilis, the following eventualities may occur: (1) a permanent arrest of the infection, (2) a temporary arrest with renewed activity within two years and, (3) a failure to arrest the infection even temporarily. Only a proper spinal fluid examination gives a clue to these three alternatives. On the basis of their observations no relapse occurred later than two years after the arrest of the inflammatory process. Penicillin proved to be the treatment of choice.

Spiller and Stewart treated 170 patients with neurosyphilis. Of these, 122 patients were observed for more than one year and 78 for two or more years. The authors find the clinical evaluation of improvement in neurosyphilis sometimes difficult and subject to inaccuracies. Of the larger groups of patients treated with penicillin alone, 100 (or 95 per cent) showed improvement in spinal fluid abnormalities, whereas 64 (or 98 per cent) of the patients given penicillin plus malaria showed the same results. Of the penicillin alone group, 5 per cent showed relapse in the spinal fluid against 2 per cent of the malaria plus penicillin group. The authors find the clinical response and the improvement of spinal fluid findings equal and extremely gratifying in both groups.

Callaway et al. report on 207 patients with various forms of neurosyphilis. Included were patients observed for more than one year. Of the 77 patients with asymptomatic neurosyphilis, 67 received penicillin alone and 10 patients penicillin plus malaria. Optimal results were obtained in 24 per cent of the patients treated with penicillin alone and 10 per cent (!) of the 10 patients treated with penicillin plus malaria. Of all the patients, 34.8 per cent returned to "near normal," 42 per cent showed moderate improvement, while 23.2 per cent received little or no benefit from therapy. Combined penicillin and fever therapy did not prove more effective than penicillin alone in a dosage of 4 to 6 million units. Patients with symptomatic paresis responded best while those with congenital central nervous system syphilis responded less favorably. Two patients with syphilitic spastic paraplegia remained unimproved and one patient with meningo-

myelitis showed only moderate improvement. The laboratory tests in the group of improved patients became "normal" within three to six months after treatment except for the spinal fluid Wassermann and the colloidal mastic reaction which remained positive for prolonged periods.

Curtis et al. attempt a post-treatment evaluation four to five years following penicillin alone and penicillin plus malaria. From the analysis of 430 patients of whom 221 had received penicillin alone and 209 penicillin plus malaria, the authors conclude that "penicillin alone is adequate in all types of neurosyphilis except severe paresis and possibly primary optic atrophy." The reported data, however, do not support the exceptions made in the above statement. "Little or no overall difference in the spinal fluid response" was seen in both groups. The only evidence of the superior effect of combined therapy in patients with paresis or taboparesis followed for four or five years is the fact that the Kahn test of the spinal fluid became negative in 23 per cent of the 22 patients treated with penicillin alone as contrasted with 40 per cent of the 35 patients treated with penicillin plus malaria. Even if one would accept these small figures as statistically significant one would still have to challenge the value of a negative Kahn test as a criterion of "superior" therapeutic effectiveness as long as the other tests of the spinal fluid give identical results in both groups.

Dattner, Thomas and de Mello treated 555 patients with various forms of neurosyphilis with penicillin alone. Of these patients, 117 could not be followed up long enough to be considered for their study. Of the remaining 438 patients, of whom 255 have been observed for more than two years and 355 for more than one year, 400 became and remained inactive as determined by spinal fluid tests. Of the 38 failures, only 31 were re-treated by the authors; 25 were re-treated only once; three, twice; and three, three times. Of the 31 re-treated patients, 27 had inactive spinal fluids when last examined; two had not yet been followed up for six months after re-treatment; one failed to respond to a second retreatment and went elsewhere for care; and one had still marked pleocytosis and abnormal colloidal gold reactions but negative spinal fluid Wassermann tests after a third re-treatment. In a later paper, Dattner reports on the successful arrest of the neurosyphilitic process in the first two cases and on the definite failure of treatment in the last case. Dattner and his co-workers, consider penicillin alone in a total dose of at least six million units given over a period of 15 to 19 days as effective therapy in all forms of neurosyphilis. If the first treatment fails another attempt with penicillin in a higher dosage offers good prospect of success.

Brown in a five-year study of 50 patients with advanced dementia paralytica favors a combination of penicillin with therapeutic malaria. A closer analysis of his material, however, fails to prove his point. Fifty

patients were subjected to five different methods of treatment, so that only 10 patients received penicillin alone. Group I (penicillin only) received not more than four million units of penicillin, partly amorphous water soluble and partly crystalline potassium G penicillin in dosages of 20,000 units every two hours for $16\frac{2}{3}$ days. It is quite obvious that at the present time four million units of penicillin cannot be considered an adequate amount for the treatment of advanced paresis and, therefore, no valid conclusions with regard to the effectiveness of penicillin alone can be drawn from Brown's study.

Johnwick tried to determine whether the therapeutic results can be enhanced by the addition of arsenicals and bismuth to a schedule using penicillin. Eight hundred seventy-nine neurosyphilitic patients were treated with these two schedules. No patients with severe psychosis were included. There were 619 patients in the penicillin alone group and 260 in the group who received penicillin and, in addition, eight injections of mapharsen and five injections of bismuth. Of the patients on the combined schedules, 88 had early asymptomatic neurosyphilis, 103 late asymptomatic neurosyphilis, 22 general paresis, 37 tabes, none taboparesis and 10 meningovascular syphilis. The corresponding figures for the group receiving penicillin alone are 94, 228, 87, 105, 18 and 87. Signals for re-treatment were based on laboratory examinations. The re-treatment rate for the combined group was almost three times as high over an 18-month period as for the group treated with penicillin alone. The total number of patients re-treated were 16 of the 619 patients originally treated with penicillin alone and 21 of the 260 given combined treatment. It appeared from the study to Johnwick that nothing was gained by the addition of mapharsen and bismuth to penicillin. Before the entire group of patients had been collected the administration of arsenicals was discontinued which accounts for a greater number of patients having been subsequently assigned to the schedule containing penicillin alone.

Epstein and Allen combined penicillin with fever induced by the blanket method for the treatment of 81 patients with various forms of neurosyphilis. Most of the patients received six million units, 300,000 units daily for 20 injections—some a somewhat higher dose, from nine to ten million units. Artificial fever consisted of four to five episodes with temperatures of $104-105^{\circ}$ F. of five hours duration. Simultaneously with the fever the patients were treated with penicillin. Of 30 patients with general paresis or taboparesis, 22 were considered to have had a satisfactory therapeutic response, and of these, 17 were thought to be greatly improved. Therapeutic response in the six tabetic patients was not striking. The five cases with meningovascular syphilis were greatly improved. Of 12 patients with primary optic atrophy of varying degrees one showed decided improve-

ment in vision, three moderate, four showed arrest of progression and four got worse. Of all patients with active spinal fluids at the beginning of therapy, 94.8 per cent showed inactivation according to the Dattner-Thomas formula. It was, however, the impression of the authors that the clinical response was better when fever was added to penicillin, particularly in the treatment of patients with dementia paralytica, optic atrophy and meningovascular syphilis. The author did not, however, establish comparative series of patients treated with penicillin only.

Rose and Carmen report on clinical follow-up studies on 130 cases of long standing parietic neurosyphilis treated with penicillin. All patients had been hospitalized for an average of 22 months prior to the administration of penicillin. Each had previously received bismuth, mapharsen, and/or tryparsamide. Of the 104 patients who received fever therapy plus penicillin, 46 (44 per cent) returned to the community, 52 are still in the hospital and 6 are dead. Of the 26 patients treated with penicillin alone, 8 (30 per cent) were returned home, 12 are still in the hospital and 6 are dead. In summary, 54 (42 per cent) patients are in the community, 64 (49 per cent) remain hospitalized and 12 (9 per cent) are dead two and a half to six years following therapy. It is reasoned that, prior to the use of penicillin, patients with general paresis of that duration and severity would not have shown arrest of the process in that percentage. All patients received penicillin intramuscularly every three hours over 15 days in amounts ranging from three to nine million units.

Perlo, Rose, Carmen and Solomon compare the results of treatment with penicillin alone and penicillin combined with malaria therapy in 469 patients. The report covers 365 patients followed for one to six years. The majority were psychotic. Seventy-three per cent were general parietics, and 32 per cent of these were treated with penicillin alone, the remainder with combined therapy. Penicillin dosage was three million units in 31 per cent, six to nine million in the remainder. Re-treatment was necessary in 26 per cent of the patients treated with penicillin alone against 17 per cent of those who received combined therapy. Clinical improvement was obtained in 58 per cent of the 365 patients. The authors conclude: "Overall results in patients treated with penicillin alone are distinctly superior to those obtained with combined treatment. . . . On the basis of the six year follow-up, penicillin alone appears to be at least as effective as combined fever and penicillin in the treatment of all types of neurosyphilis. Effectiveness of treatment was reflected in rapid improvement in the spinal fluid in all adequately treated cases within several months after treatment. Approximately 32 per cent of the patients still have group II spinal fluids one to six years after treatment. However, the persistent abnormalities in almost all of the cases are limited to positive serologic and gold sol reactions

and do not indicate activity in the spinal fluid." Thus, Perlo and co-authors have reversed themselves on the issue of combined therapy for general paresis and have finally confirmed the concepts and experiences of Dattner and Thomas. However, they still have some reservations. "Although penicillin alone can be recommended as the treatment of choice for all forms of neurosyphilis on the basis of the results in this study, it may be premature to discard fever entirely as an adjunctive therapy. A follow-up of longer duration must still be carried out in order to compare the effectiveness of penicillin alone with combined penicillin fever therapy in terms of ability to protect the central nervous system against premature degenerative changes." Since their six-year observation exceeds the usual five-year life expectancy of an untreated paretic and exceeds the time after treatment during which relapses are noted it seems that the authors are unnecessarily strict in their standards of evaluation.

The same ambiguity is discernible in the paper of Hahn which offers an extensive analysis of a total of 589 patients with neurosyphilis. Four hundred seventy-nine were treated initially with penicillin alone and 110 with penicillin plus malaria. In retrospect, it is difficult for Hahn to determine the precise reasons for the particular treatment regime selected in a given case. Private patients were more frequently treated with malaria plus penicillin and clinic patients with penicillin alone. White patients more frequently received malaria plus penicillin and Negroes penicillin alone. The number of patients in any one diagnostic category treated by any particular schedule is too small to be of statistical significance. Although the determination of incidence of re-treatment seemed to be a possible method of estimating the therapeutic efficacy of a given treatment, it is an imperfect criterion in Hahn's material because there was a greater tendency to re-treat after a relatively new method of therapy such as penicillin as compared with the older and well proved malaria therapy. If the spinal fluid relapse rate is taken as an index of therapeutic results, both groups show almost identical figures, 1.25 per cent for the penicillin group and 0.93 per cent for the other. No patients with an inactive (less than 10 cells!) initial spinal fluid suffered a spinal fluid relapse. All seven relapses which occurred were observed within the first two years only. Good spinal fluid results in parenchymatous neurosyphilis were obtained with either method. No advantage of malaria therapy in a small group of three patients who were re-treated because of spinal fluid failure after penicillin alone, was seen. The work status of 74 paretics and taboparetics treated with penicillin alone was compared with that of a similar group of patients treated with penicillin plus malaria. The results of both methods were essentially the same. Complete rehabilitation was achieved for 46 per cent of the penicillin group and 44.2 per cent of the penicillin plus

malaria group and partial rehabilitation for 18.9 and 18.6 per cent, respectively. Of the penicillin group, 10.8 per cent, and of the penicillin plus malaria group 9.3 per cent were unable to work. Another method of clinical evaluation, based largely on repeated mental status examinations, revealed a definite though slight advantage for the penicillin plus malaria group. Treatment failure occurred in 33.8 per cent of the penicillin group as compared with 16.3 per cent of the other group. With respect to physical signs of neurosyphilis both methods were equally effective. Progression was noted in 6 of 17 patients with primary optic atrophy after treatment with penicillin alone, and in 3 of 16 after treatment with penicillin plus malaria. Because penicillin alone cannot yet be evaluated the author suggests penicillin and malaria as the treatment of choice. Severe tabetic symptoms did not disappear following either method of treatment. Increment in body weight is almost identical in all types of neurosyphilis after both methods of treatment. In *tabes dorsalis* the results of any form of treatment are difficult to evaluate. Penicillin alone effected the disappearance of mild to moderate tabetic symptoms in approximately one-third of the patients treated. Severe symptoms did not disappear completely. As judged by overall clinical results, the addition of malaria therapy to penicillin does not afford a definite additional benefit. Penicillin alone is effective therapy in paresis and the paretic component of taboparesis. The addition of malaria therapy may afford slight additional benefit with respect to clinical results but no definite conclusions can be drawn as to this point. Hahn, too, stresses the relative brevity of observation period and considers the present study only as a progress report. To the reviewers it seems questionable whether a longer follow-up will add much to the information obtained.

Ingraham, Jr. et al. deal with the spinal fluid response following penicillin therapy, including a comparison with prepenicillin therapy in 603 cases of neurosyphilis observed for varying periods into the seventh year after treatment. In all types of neurosyphilis, the spinal fluid response is most rapid during the first year, and the maximal response is obtained between the third and fourth year. By the fifth year, normal or near normal (i.e., inactive) spinal fluids may be expected in 50 per cent of patients with paresis and taboparesis, and in 70 per cent of those with *tabes*. These figures are much too low and are not in agreement with any others reported in the literature. It is also surprising to the reviewers that spinal fluid relapse after the 3rd or 4th year occurred in as many as 5 per cent of their tabetics and paretics. At Bellevue Hospital not a single such case was seen two years after treatment. Analysis of results in 146 patients treated in prepenicillin days indicates that the spinal fluid response from penicillin is more rapid and reaches its maximum effect a year or two earlier than that from metal therapy and fever.

Klauder studied 397 patients with primary optic atrophy. On admission 17 per cent had only light perception or less and 44 per cent had visual acuity of $\frac{1}{80}$ to $\frac{6}{80}$, in other words, 61 per cent of the patients when first seen were either essentially or industrially blind. The author, therefore, stresses that an ophthalmologic examination should be conducted in every patient who has neurosyphilis when first seen and this by perimetric field studies. Klauder is in favor of a combination of penicillin with fever produced by malaria rather than by intravenous vaccine. If there is evidence of unfavorable progress, Klauder advises re-treatment with penicillin and continuous treatment with metal chemotherapy. Some patients received as many as four different courses of penicillin. Of 80 patients treated as stated, 48 remained unchanged during 12 to 78 months, 15 got worse within 4 to 70 months and 15 got blind within 3 to 30 months. These results are considered gratifying by the author since about 50 per cent of the patients were industrially blind at the onset of treatment. One regrets that Klauder did not avail himself of a series of patients treated with penicillin alone. He would then have had a stronger argument in favor of his rather rigorous therapy, since there is considerable evidence that penicillin alone would have produced the same favorable results.

Jones et al. subjected 19 patients with non-tabetic spinal cord syphilis to penicillin therapy. In five patients with mild to moderately severe diffuse meningovascular syphilis of less than three months duration excellent results were obtained. Little or no improvement occurred in patients with myelomalacia from vascular occlusion or in patients with degenerative changes caused by long standing spinal cord damage. Little improvement was seen in two cases of Erb's spastic paraplegia and one with amyotrophic lateral sclerosis. Fatalities and poor results were often related to complications such as decubital ulcers, urinary tract infections and contractures of paretic limbs.

In the English literature there is only one paper dealing with a large group of patients treated with penicillin. Nicol and Whelen had a rather extensive experience with malaria therapy before the advent of penicillin and compare the results of penicillin alone, malaria alone and penicillin plus malaria. Unfortunately, the group of patients treated with penicillin alone comprises only 31 patients and, therefore, the authors are unable to draw valid conclusions as to the merits of pure penicillin therapy. But in their evaluation of malaria therapy alone and malaria plus penicillin the advantage of penicillin is quite obvious. Of the 152 patients treated with penicillin plus malaria 86.5 per cent were alive at the end of three years, whereas of the 280 cases treated with malaria alone there were only 69 per cent. The authors observed one death following penicillin therapy which they consider was due to a Herxheimer reaction. A 62-year-old

confused paretic who was in very poor physical condition, received 300,000 units penicillin intramuscularly daily. Forty-eight hours after the first injection he began to have seizures, which continued intermittently until his death 24 hours later. One patient with the galloping form of paresis died in spite of daily injections of 300,000 units penicillin in a total amount of 4,200,000 units. As mentioned before, this type of general paresis requires much larger dosages of penicillin.

Of the newer antibiotics, aureomycin was given orally to 12 patients with neurosyphilis by Kierland and O'Leary. Ten of these patients have been observed for periods varying from 122 to 573 days. Nine additional patients have received similar treatment with equally good results. In all cases there has been a continued improvement in spinal fluid findings and all patients with exception of one have shown moderate to marked degrees of clinical benefit. Among the patients treated were one taboparetic and five paretics. The one failure occurred in a paretic. Approximately 60 Gm. of aureomycin, with 2 to 4 Gm. given daily in divided doses, is sufficient for a single or first course of therapy. The authors feel that aureomycin is equal to penicillin in the treatment of neurosyphilis.

At the International Symposium on Syphilis of the World Health Organization held in Paris, 1950, Baudouin and Lereboullet reported on the formerly mentioned decrease in incidence of neurosyphilis observed in France during the past 20 years. This appears to be due to the progress made in diagnosis and treatment of primary and secondary syphilis. Before the advent of penicillin the therapy practiced in France consisted of an initial treatment with arsenic or bismuth or both, and a "consolidation treatment" which was continued over a number of years. The dangers of the arsenobenzols led most experts to discontinue their use. Since bismuth does not have the same disadvantage, many French doctors hesitated to abandon it in favor of a new therapy until there had been a sufficient time lapse to prove the value of such new treatment. The French authors believed that at least 15 to 20 years of observation were needed, since this is the average period between the appearance of the chancre and the first signs of tabes and general paresis. These remarks characterize the attitude of the French toward the penicillin treatment of neurosyphilis. The authors are strongly in favor of malaria therapy plus penicillin in general paresis and bismuth and arsenic plus penicillin in alternating courses for tabes dorsalis. These conclusions are based on statistics assembled mostly from the American and partly from the French literature.

Canelas at the University of São Paulo subjected 50 patients with neurosyphilis to various methods of treatment. Ten patients received malaria plus arsenic, 21 penicillin plus fever and arsenic, 13 penicillin alone, 3 penicillin plus fever and 5 arsenic only. The results were evaluated

by spinal fluid findings. The author concludes from his study that considering the dangers involved in malaria therapy penicillin alone is the treatment of choice for neurosyphilis if given in doses of 10 to 15 million units.

Gammon et al. autopsied seven cases of neurosyphilis. One parietic who died three weeks after treatment showed the usual histologic picture; the others showed typical ganglion cell loss but little lymphocytic infiltration. The authors state that the diagnosis of syphilis might have been in doubt except for the associated degeneration.

Gädeke failed to find any histologic evidence of syphilitic infection in a parietic who came to autopsy 25 years after the onset of his disease. The patient has had five bouts of relapsing fever as the only treatment in 1920. Clinical improvement set in and in 1928 the serologic reactions became negative. He died from hypertension and cardiac failure in 1946.

Simma examined nine parietic brains looking for histologic changes in the thalamus. Inflammatory reactions were present in all cases in various degrees but less massive than those seen in the frontal cortex. In addition, some degenerative changes considered to be secondary and retrograde were also seen in the oral, middle and posterior parts of the thalamus.

REFERENCES

- Baudouin, A. and Lereboullet, J.: Le traitement prophylactique et curatif de la syphilis nerveuse. *Prophylax. antivén.* 22:428-442, 1950.
- Brown, P. N.: Efficacy of aqueous penicillin alone and combined with other methods in advanced dementia paralytica, a 5 year Study. *Arch. Neurol. & Psychiat.* 66:464-469, 1951.
- Bush, S. K.: A fatal Herxheimer reaction in a case of neurosyphilis. *Am. Practitioner.* 1:1183-1185, 1950.
- Callaway, J. L., Flower, A. H. Jr., Hirschmann, V. R., and Olansky, S.: A four-year study of penicillin treatment of syphilis of the central nervous system. *South. M. J.* 43:412-422, 1950.
- Canelas, H. M.: Resultados terapêuticos em 50 casos de neurosifilis. *Arq. neuropsiquiat.*, São Paulo, 9:21-31, 1951.
- Curtis, A. C., Kruse, W. T., and Norton, D. H.: Neurosyphilis IV. Post-treatment evaluation 4 to 5 years following penicillin and penicillin plus malaria. *Am. J. Syph., Gonorr. & Ven. Dis.* 34:554-565, 1950.
- Curtis, A. C., Kitchen, D. K., O'Leary, P. A., Rattner, H., Rein, C. R., Schoch, A. G., and Shaffer, L. W.: Penicillin treatment of syphilis. *J.A.M.A.* 145:1223, 1951.
- Dattner, B.: Follow-up report on penicillin failures in neurosyphilis. *Am. J. Syph., Gonorr. & Ven. Dis.* 34:373-77, 1950.
- , Thomas, E. W. and de Mello, L.: Results of penicillin therapy for neurosyphilis at Bellevue Hospital. *J. Ven. Dis. Inform.* 32:33-39, 1951.
- , Thomas, E. W. and de Mello, L.: Criteria for the management of neurosyphilis. *Am. J. Med.* 10:463-467, 1951.
- : Diagnostic and therapeutic problems in neurosyphilis. *Acta dermat.-venereol.* 31:111-119, Suppl. 24, 1951.

- Epstein, W. N. and Allen, J. R.: Treatment of neurosyphilis with penicillin combined with artificial fever therapy. II. Further observations. *Arch. Dermat. & Syph.* 63:419-425, 1951.
- Ford, W. J., Wiggall, R. H., and Stokes, J. H.: Penicillin therapy of asymptomatic neurosyphilis. The spinal fluid cell count as a guide to therapeutic response and re-treatment. *Arch. Int. Med.* 88:235-242, 1951.
- Gädeke, R.: Das morphologische Bild einer Klinisch "Geheilten" Progressiven Paralyse 25 Jahre nach der Floriden Erkrankung. *Deutsche Ztschr. Nervenhe.* 165:482-487, 1951.
- Gammon, G. D., Lewey, F. H., Villon, H., Schwarz, G., and Stokes, J. H.: Pathologic observations of penicillin-treated neurosyphilis. *Am. J. Syph., Gonorr. & Ven. Dis.* 34:227-235, 1950.
- Hahn, R. D.: The treatment of neurosyphilis with penicillin and with penicillin plus malaria. *Am. J. Syph., Gonorr. & Ven. Dis.* 35:433-471, 1951.
- Ingraham, N. R., Jr., Stokes, J. H., and Gammon, G. D.: Penicillin alone in neurosyphilis: Spinal fluid response including a comparison with prepenicillin therapy. *Am. J. Syph., Gonorr. & Ven. Dis.* 34:566-581, 1950.
- Johnwick, E. B.: The treatment of neurosyphilis: Penicillin alone versus penicillin plus arsenic and bismuth. *J. Ven. Dis. Inform.* 31:303-308, 1950.
- Jones, R. W., Jr., Heyman, A., Smith, W. A., and Wilson, R.: Penicillin therapy of nontabetic spinal cord syphilis. *Am. J. Syph., Gonorr. & Ven. Dis.* 35:72-78, 1951.
- Klauder, J. V.: Blindness due to syphilis. *J. Ven. Dis. Inform.* 32:183-192, 1951.
- and Meyer, G. P.: Early diagnosis of syphilitic primary optic nerve atrophy. *Arch. Ophth.* 43:537-552, 1950.
- Kierland, R. R. and O'Leary, P. A.: Oral treatment of neurosyphilis with aureomycin. Progress Report *Am. J. Syph., Gonorr. & Ven. Dis.* 35:544-553, 1951.
- Moragues, V. and Wyatt, J. P.: Fatal hemoglobinuric nephrosis following intrathecal penicillin in neurosyphilis. *Am. J. Syph., Gonorr. & Ven. Dis.* 34:177-181, 1950.
- Nicol, W. D. and Whelen, M.: Penicillin in the treatment of neurosyphilis. *Brit. J. Ven. Dis.* 27:132-141, 1951.
- Nielsen, J. P.: Follow-up of syphilitics. Late manifestations in 467 male patients with early syphilis followed for 29-36 years. *Acta dermat.-venereol.* 30:507-512, 1950.
- Noojin, R. O., Pace, B. F., and Praytor, H. B.: Prolonged fever produced with 3 injections of typhoid vaccine. *Am. J. Syph., Gonorr. & Ven. Dis.* 34:153-160, 1950.
- Packer, H.: Problems and their management in central nervous system and cardiovascular syphilis. *Am. Pract. & Digest. Treat.* 2:422-27, 1951.
- Perlo, V. P., Rose, A. L., Carmen, L. R., and Solomon, H. C.: The treatment of neurosyphilis—one-to-six year follow-up of patients treated with penicillin at the Boston Psychiatric Hospital. Comparison of results with penicillin alone and combined penicillin and malaria therapy. *Am. J. Syph., Gonorr. & Ven. Dis.* 35:559-568, 1951.
- Putkonen, T. and Rehtijärvi, K.: Febrile Herxheimer reaction in neurosyphilis. *Acta. dermat.-venereol.* 31:120-132, Suppl. 24, 1951.
- Rose, A. L. and Carmen, L. R.: Clinical follow-up studies on 130 cases of long-standing parietic neurosyphilis treated with penicillin. *Am. J. Syph., Gonorr. & Ven. Dis.* 35:278-283, 1951.

- Shapiro, L. K. and Berris B.: The dangers of penicillin therapy in syphilis of the central nervous system. With special reference to the occurrence of delayed reactions. *Minnesota Med.* 34:141-144, 1951.
- Simma, K.: Über Thalamusveränderungen bei Progressiver Paralyse. *Monatschr. f. Psychiat. u. Neurol.* 121:297-302, 1951.
- Smith, R. H. F.: Permeability of the blood-brain barrier to penicillin in cases of parenchymatous neurosyphilis. *J. Ment. Sc.* 97:340-361, 1951.
- Spiller, W. F. and Stewart, J.: Neurosyphilis: Comparable treatment with penicillin alone and penicillin plus malaria. *J. Invest. Dermat.* 14:121-131, 1950.
- Stewart, R. M.: G.P.I. Its juvenile and senile types. *Edinburgh M. J.* 7:17-29, 1950.
- Willcox, R. R.: Some observations on neurosyphilis in the African Negro. *J. Ven. Dis. Inform.* 32:229-237, 1951.
- : Syphilitic mental disease in the African Negro. *J. Roy. Army M. Corps.* 97:97-110, 1951.
- Wright, R. D., Thayer, J. D., Nicholson, F. P., and Arnold, R. C.: Penicillin levels in spinal fluid after intramuscular injection of procaine penicillin. *J. Ven. Dis. Inform.* 32:39-43, 1951.

Pediatric Neurology

By HENRY W. BAIRD, III, M.D.

BIRTH INJURY. Craig¹¹ points out the difficulty in making the diagnosis of an intracranial lesion in the newborn infant. Irrespective of the extent of the lesion, he found the most constant clinical sign to be unnatural alertness and awareness, an expression usually seen only in older infants. The immediate and long term prognosis of cerebral injury in the newborn infant is discussed in detail. Of the 593 children seen by the author over a period of 17 years, in whom the diagnosis of intracranial irritation had been made, only 52 had demonstrable mental or physical defects. The most common physical disability found in later life was hemiplegia. Familial, hereditary, and developmental factors which might be related to cerebral damage were excluded in so far as possible.

In the absence of infection, Craig's recommendations for immediate treatment include minimal disturbance of the infant, omission of lumbar puncture, and adequate sedation with chloral hydrate, 60 mgm. each half hour until violent symptoms are controlled. Expert nursing is also stressed. In a previous publication Craig has discussed the pathologic correlations with the diagnostic clinical findings.¹⁰

The late effects of cerebral birth injury are reviewed by McKhann et al.²⁰ In 53 per cent of 412 cases of mental retardation, convulsive disorders, or cerebral palsy, birth injury (late prenatal or paranatal) was thought to be the causative factor. The authors did not distinguish between cerebral birth injuries caused by anoxia and those caused by direct trauma. Behavior disturbances without mental retardation, spasticity, or convulsions were considered possible sequelae of milder degrees of cerebral injuries at birth.

Campbell, Cheeseman, and Kilpatrick³ report a follow-up study on a group of 89 children with a history of anoxia; 178 children with no such history were used for controls. The results of their examinations do not support the theory that asphyxia neonatorum is a common cause of mental or physical retardation.⁸

Cerebral Palsy. Increasing interest has been shown in the problem of cerebral palsy. Bakwin and Bakwin⁶ present a concise summary of current thought. The physiologic basis of cerebral palsy was the subject of the

first symposium on cerebral palsy sponsored by the United Cerebral Palsy Fund.³¹ In a well documented article, Denhoff, Smirnhoff, and Holden state that cerebral palsy should be considered a syndrome of brain damage rather than a separate disease entity.¹⁶ The emotional handicaps of both parents and children are stressed, and it is concluded that a medically supervised team of specialized workers is essential for proper management of the problem.

Denhoff and Holden¹⁴ stress the recognition of slow development as an aid to the early diagnosis of cerebral palsy. They suggest a possible correlation between delay in speaking sentences of two and three words and retarded intellectual function.

Hydrocephalus. A case of hydrocephalus associated with intrauterine meningitis has been reported.¹² The possible etiology is discussed in detail. Bogdan reports a syndrome consisting of microcephaly, chorioretinopathy, cerebral calcification, and internal hydrocephalus similar to that observed in toxoplasmosis, but distinguished by antibody fixation tests.⁷

Radioactive phosphorus (P^{32}) has been used as a tracer substance by Adams¹ in studies dealing with the cerebrospinal fluid flow in normal and hydrocephalic patients. The dynamics of normal CSF both in man and in the dog are associated with reasonably constant curves for uptake and disappearance of P^{32} . In four hydrocephalic infants, a decreased rate of uptake and a decreased rate of disappearance were found. In two hydrocephalic infants in whom the dynamics were normal, it was suspected that there was an overproduction of fluid rather than a defect in absorption.

The surgical treatment of hydrocephalus is receiving increasing attention since non-irritant plastic materials such as "portex" have become available for shunt procedures. Jackson has reviewed the subject in some detail.¹⁹ Various operations have been described, such as the third ventriculostomy of Voris,⁴⁰ puncture of the lamina terminalis and floor of the third ventricle by Scarff,³⁶ and ureterosubarachnoid anastomosis.¹³ Patients treated by the last procedure must be carefully observed for electrolyte imbalance.^{28a}

The use of ethylene in pneumoencephalography is discussed by Aird and Zealer² in a paper concerned with mechanisms causing obstructions to the flow of cerebrospinal fluid. They summarize their results in 630 patients without commenting on their ages. In patients with a history of meningoencephalitis or with a brain tumor, the disappearance of the gas was frequently delayed. The hypothesis is presented that space-obliterating processes may be as important as space-occupying lesions in the production of subarachnoid block, impairment of CSF circulation and increased intracranial pressures. The authors conclude that the rate of disappearance of ethylene is a relatively sensitive test for the detection of a partially obstructive process.

Rh Iso-Immunization. The role of the Rh factor in mental deficiency is discussed by Glasser, Jacobs and Schain.¹⁷ They suggest that Rh sensitization of the mother may lead to mental deficiency in the child even in the absence of definite hemolytic symptoms at birth.

Erythroblastosis fetalis is only one factor that may be responsible for kernicterus. Arey and Dent³ report the presence of kernicterus in eight premature infants, in seven of whom the pathologic findings did not justify a diagnosis of erythroblastosis fetalis. Even though erythroblastosis was not excluded by immunologic methods, the observations suggest that the kernicterus in at least some of these infants was not related to erythroblastosis fetalis.

*Convulsive Disorders.** Yannet, who discusses both drug therapy and the importance of psychogenic factors, describes a sound approach to the treatment of the convulsive state in children.⁴³ A detailed plan of therapy including dosages of drugs employed is presented as is a review of the general problems to be considered in management.

Psychomotor epilepsy alone was found in 16 of Lennox's series of 410 children with convulsive disorders below the age of four years. In an additional 24 patients, psychomotor epilepsy was associated with grand and/or petit mal seizures. The symptomatology, differential diagnosis and treatment of such patients are outlined.²⁵

Livingston²⁶ discusses abdominal pain as a manifestation of epilepsy. In his series, the diagnosis of abdominal epilepsy was made when the child had an abnormal EEG, recurrent abdominal pain often followed by sleep, and a response to anticonvulsant medication. The incidence of this syndrome is not known, but it may be important in the differential diagnosis of abdominal pain in children, especially when it is associated with disturbances of behavior.

The rationale for the use of anticonvulsant drugs in children with behavior problems is presented by Pasamanick.³² He reviews his results in 21 hospitalized boys of 6 to 13 years of age with behavior problems and abnormal electroencephalograms. With minor exceptions no significant improvement in behavior was noted after administration of various anticonvulsant drugs. However, the administration of amphetamine produced improvement in some children. The author ascribed the beneficial effect of amphetamine to its influence on the poorly integrated neural associations of such children rather than to any specific anticonvulsant property.

Krynauw^{23, 24} reports the result of hemispherectomy in 20 patients with infantile hemiplegia. Benefit was observed in patients with hemiplegia combined with convulsive symptoms, mental changes or an epileptic equivalent,

* Only papers not reviewed in Chapter 10 are mentioned here.

such as episodic outbursts of violent temper tantrums. There is said to be a decrease in the number of convulsions, improvement in the patient's sense of well being, and apparent improvement in intelligence after removal of the damaged hemisphere. He suggests that the natural physiologic activities of the normal side may be disrupted by an overflow of grossly abnormal waves from the impaired side. EEG evidence is presented in support of this theory. Such theories are interesting but highly speculative.

*Electroencephalography.** The electroencephalographic findings accompanying various conditions have become increasingly useful as diagnostic aids in the pediatric age group. Topper³⁹ suggests that the EEG findings in children with congenital hypothyroidism can often be correlated with the prognosis. The results of a five hour glucose tolerance test have been correlated with EEG findings in possible hypoglycemia by Ross and Loeser.³⁵ After fasting specimens of blood had been drawn for sugar determinations, their patients were given an oral dose of glucose. Blood samples were taken $\frac{1}{2}$ hour and 1, 2, 3, 4, and 5 hours after ingestion of glucose. EEGs were recorded after each blood sample, both at rest and after 3 minutes of hyperventilation. The authors believe that the results of the five hour tolerance test together with the EEG findings are helpful in the management of hypoglycemia. Anticonvulsant medication as well as a high protein multiple feeding diet is recommended in cases which develop a cerebral dysrhythmia during the five hour glucose tolerance test.

Congenital Anomalies. McKeown and Record²⁹ report a significantly higher incidence of congenital malformations of the central nervous system during the period October through March than from April through September. First births showed a higher incidence of malformation than later ones. No history of infectious diseases was elicited in these cases. The same authors report data obtained from 69 pairs of twins. The incidence of malformation of the central nervous system in a single twin was found to correspond with that of siblings of different pregnancies.³³ This work emphasizes the importance of hereditary factors in congenital malformations.

Intracranial complications of congenital dermal sinuses include meningitis, abscess formations, osteomyelitis and hydrocephalus. The presence of a dimple or subcutaneous mass in the midline is commonly associated with such a sinus. The dimple may be demonstrable only after careful examination of the shaved head. If roentgenographic films reveal a skull defect, operative removal is indicated, since excision after infection has occurred is difficult.²⁸

Neoplasms. Arnstein, Boldrey and Naffziger⁵ review a series of patients in whom diagnoses of intracranial neoplasm were established during the

* Only papers not reviewed in Chapter 13 are mentioned here.

neonatal period and report an additional case. Hydrocephalus, although not invariably present, was the most common finding with intracranial neoplasms occurring during this age period. The majority of the neoplasms were supratentorial gliomas.

Infectious Diseases. The increasing rate of recovery of patients with proven bacterial meningitis has led to greater interest in the sequelae of infections of the central nervous system. The presence of subdural effusions has been established as a frequent complication of bacterial meningitis.^{4, 22, 38} Smith, Dormont, and Prather³⁸ reported on 20 instances of subdural effusions following meningitis in infants under 14 months of age. There was no correlation between any particular organism and the presence of subdural fluid.

The possible relationship between poliomyelitic paralysis of a single limb and a recent injection of an antigen into the limb was noted by British, American, and Australian workers in 1950. Among 2709 examples of poliomyelitis in the Minnesota outbreak of 1946 there was a high degree of correlation between the localization of the paralysis and the site of injection of antigen.⁴² There was no correlation with any particular antigen, and injections preceding the onset of the paralysis by more than one month had no effect on the localization of the paralysis.

Miscellaneous. Four instances of familial degeneration of the cerebral gray matter in childhood are discussed by Ford, Livingston, and Pryles.¹⁶ The outcome is fatal, and the course is marked by convulsions, myoclonic spasms, spasticity, choreoathetosis, cerebellar ataxia and dementia.

Shanks³⁷ discusses the syndrome of cerebellar ataxia in children with emphasis on instances in which a neoplasm is not found. The most valuable point in distinguishing benign from progressive lesions was found to be the mode of onset. Thirty-nine instances, 30 of whom were traced, are discussed. When the onset was sudden, the course was almost always benign, whereas the disease was progressive when the ataxia began insidiously.

Mental retardation, as measured by currently available tests, is not improved by the carotid-jugular anastomosis operation.²¹ The sources of confusion in the evaluation of a retarded child are clearly outlined.

Lewis^{25a} deals with the problem of brain injury in children. The aspects of psychopathology, management and education are discussed.

Rostral dominance in children was tested by Cohn;⁹ for example, light pinprick of the left shoulder and the right hand would be noted on the left shoulder if such a dominance were present. Under the age of six years, rostral dominance is usually present.

Reiner³⁴ discusses a reflex which consists of fisting and flexion of the arms. It occurs when the human infant is held by the ankles any time between the 36th fetal week and the 40th postpartum week. After the 40th week this reflex, which he calls the tonic symmetry of the inverted human infant,

disappears but returns when the infant becomes tired, toxic, or hungry. Its value as a diagnostic sign is not known.

REFERENCES

- ¹ Adams, J. E.: Tracer studies with radioactive phosphorus (P^{32}): on the absorption of cerebrospinal fluid and the problem of hydrocephalus. *J. Neurosurg.* 8:279-288, 1951.
- ² Aird, R. B. and Zealer, D.: Pneumoencephalographic study of cerebrospinal-fluid absorptive-block mechanisms. *Arch. Neurol. & Psychiat.* 66:199-212, 1951.
- ³ Arey, J. B. and Dent, J.: Pathologic findings in premature infants. *Clin. Path.* 24:1016-25, 1950.
- ⁴ Arnold, G. G.: Purulent and serous subdural effusions in the course of purulent meningitis. *J. Ped.* 39:191, 1951.
- ⁵ Arnstein, L. H., Boldrey, E., and Naffziger, H. C.: A case report and survey of brain tumors during the neonatal period. *J. Neurosurg.* 8:315-319, 1951.
- ⁶ Bakwin, R. B. and Bakwin, H.: Cerebral palsy in children. *J. Ped.* 39:113-122, 1951.
- ⁷ Bogdan, A.: Microcephaly with chorioretinopathy, cerebral calcification and internal hydrocephalus. *Proc. Roy. Soc. Med.* 44:225-6, 1951.
- ⁸ Campbell, W. A. B., Cheeseman, E. A., and Kilpatrick, A. W.: The effects of neonatal asphyxia on physical and mental development. *Arch. Dis. Child.* 25:351-9, 1950.
- ⁹ Cohn, R.: On certain aspects of the sensory organization of the human brain: II. A study of rostral dominance in children. *Neurol.* 1:119-122, 1951.
- ¹⁰ Craig, W. S.: Intracranial hemorrhage in the newborn. *Arch. Dis. Child.* 13:89, 1938.
- ¹¹ —: Intracranial irritation in the newborn: immediate and long term prognosis. *Arch. Dis. Child.* 25:325, 1950.
- ¹² Crosby, R. M. N., Mosberg, W. H., and Smith, G. W.: Intrauterine meningitis as a cause of hydrocephalus. *J. Ped.* 39:94-101, 1951.
- ¹³ Dees, J.: Ureterosubarachnoid anastomosis for communicating hydrocephalus. *J. Urol.* 65:994-997, 1951.
- ¹⁴ Denhoff, E. and Holden, R.: The significance of delayed development in the diagnosis of cerebral palsy. *J. Ped.* 38:452, 1951.
- ¹⁵ Denhoff, E., Smirnhoff, V. N., and Holden, R. H.: Cerebral palsy. *New England J. Med.* 245:728-735, 770-777, 1951.
- ¹⁶ Ford, F. R., Livingston, S., and Pryles, C. V.: Familial degeneration of the cerebral gray matter in childhood. *J. Ped.* 39:33-43, 1951.
- ¹⁷ Glasser, F. B., Jacobs, M., and Schain, R.: The relation of Rh to mental deficiency. *Psychiatric Quart.* 25:282-287, 1951.
- ¹⁸ Gross, R. E., Clatworthy, H. W., Jr., and Meeker, I. A., Jr.: Sacrococcygeal teratomas in infants and children: a report of 40 cases. *Surg., Gynec. & Obst.* 92:341-354, 1951.
- ¹⁹ Jackson, I. J.: A review of the surgical treatment of internal hydrocephalus. *J. Ped.* 38:251-258, 1951.
- ²⁰ Kellaway, P.: The use of sedative-induced sleep as an aid to electroencephalographic diagnosis in children. *J. Ped.* 37:862-877, 1950.
- ²¹ Kessler, J. W.: Effect of carotid-jugular anastomosis operation upon intelligence. *Pediatrics.* 8:475-81, 1951.
- ²² Kinley, G., Riley, H. D., and Beck, C. S.: Subdural hematoma, hygroma, and hydroma in infants. *J. Ped.* 38: 662-86, 1951.

- ²³ Krynauw, R. A.: Infantile hemiplegia and its treatment by hemispherectomy. *Semaine d. hôp. Paris.* 1091-7, 2 April 1951.
- ²⁴ —: Infantile hemiplegia treated by removing one cerebral hemisphere. *J. Neurol., Neurosurg. & Psychiat.* 13:243, 1950.
- ²⁵ Lennox, W. G.: Phenomena and correlates of the psychomotor triad. *Neurol.* 1:357-371, 1951.
- ^{25a} Lewis, R. S. et al.: *The Other Child: The Brain-Injured Child.* New York, Grune & Stratton, 1951.
- ²⁶ Livingston, S.: Abdominal pain as a manifestation of epilepsy (abdominal epilepsy) in children. *J. Ped.* 38:687, 1951.
- ²⁷ Marcus, R. E.: Hearing and speech problems in children. *Arch. Otolaryng.* 53:134-146, 1951.
- ²⁸ Matson, D. D. and Ingraham, F. D.: Intracranial complications of congenital dermal sinuses. *Ped.* 8:463-474, 1951.
- ^{28a} —: Ventriculo-Ureterostomy. *J. Neurosurg.* 8:398-404, 1951.
- ²⁹ McKeown, T. and Record, R. G.: Seasonal incidence of congenital malformations of the central nervous system. *Lancet.* 192, Jan. 27, 1951.
- ³⁰ McKhann, C. R., Belnap, W. D., and Beck, C. S.: Late effects of cerebral birth injury. *J. Michigan M. Soc.* 50:149-152, 181, 1951.
- ³¹ Merritt, H. H.: (Summation) Symposium of cerebral palsy. *Quart. Rev. Ped.* 6:2, May 1951.
- ³² Pasamanick, B.: Anticonvulsant drug therapy of behavior problem children with abnormal electroencephalograms. *Arch. Neurol. & Psychiat.* 65:752-766, 1951.
- ³³ Record, R. G. and McKeown, T.: Congenital malformations of the central nervous system: data on sixty-nine pairs of twins. *Ann. Eugenics.* 15:285-292, 1951.
- ³⁴ Reiner, E. R.: Tonic symmetry in the inverted human infant. *Yale J. Biol. & Med.* 23:3, 1950.
- ³⁵ Ross, I. S. and Loeser, L. H.: Electroencephalographic findings in essential hypoglycemia. *EEG & Clin. Neurophysiol. J.* 3:141, 1951.
- ³⁶ Scarff, J. E.: Treatment of obstructive hydrocephalus by puncture of the lamina terminalis and floor of the third ventricle. *J. Neurosurg.* 8:204-213, 1951.
- ³⁷ Shanks, R. A.: Notes on cerebellar ataxia in childhood. *Arch. Dis. Childhood.* 25:389-91, 1950.
- ³⁸ Smith, M. H. D., Dormont, R. E., and Prather, G. W.: Subdural effusions complicating bacterial meningitis. *Pediatrics.* 7:34-43, 1951.
- ³⁹ Topper, A.: Mental achievement of congenitally hypothyroid children. *Am. J. Dis. Child.* 81:233-249, 1951.
- ⁴⁰ Voris, H. C.: Third ventriculostomy in treatment of obstructive hydrocephalus in children. *Arch. Neurol. & Psychiat.* 65:265-271, 1951.
- ⁴¹ Walker, A. E.: Treatment of epilepsy by cortical excision. *J. Ped.* 38:285-298, 1951.
- ⁴² Ward, R.: Paralytic poliomyelitis following immunizing injections. *J. Ped.* 38:781, 1951.
- ⁴³ Yannet, H.: Treatment and prognosis of convulsive disorders in children. *Bull. New York Acad. Med.* 27:466-74, 1951.

Epilepsy

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IN LAST year's review of epilepsy it was noted that the year was one primarily of retrenchment and consolidation. The period of December 1, 1950 to December 1, 1951 has again proven to be one of further consolidation. The results of this are the more definite concepts of psychomotor epilepsy, of medical therapy and of the role of subcortical structures in the genesis of epilepsy.

An important historical note has been the celebration in Denmark on December 24 of the one hundredth anniversary of the birth of Dr. Adolph Sell, the founder of epilepsy colonies in general, and most particularly, of Filadelfia.

This year has witnessed the release by the Veteran's Administration of the movie, "Seizures—The Medical Problem and Social Problems of Epilepsy." Combining as it does sound medical and surgical viewpoints with proper rehabilitatory and social factors this movie will do much to improve lay understanding of the epilepsies.

Monographs related to this field include the resumé of Penfield and Kristiansen⁸⁰ and Schwab's book on electroencephalography.⁸² The former presents an excellent compilation of Dr. Penfield's cases considered from the standpoint of clinical seizure types and the correlation with operative findings with, of course, special interest in the cortical physiology. Schwab presents electroencephalography in a concise, non-confusing manner that will do much to clarify this field for the physicians not engaged in neurology but seeking a basic understanding.

CLINICAL FACTORS

Again this year there have been reports of convulsive seizures occurring in conjunction with systemic diseases. Seizures are reported to occur as frequently as in 15 per cent of cases of lupus erythematosus⁸⁹ and the seizures may even precede the onset of the full clinical picture. For this reason the association of seizures with rheumatic arthritis or leukopenia should arouse the suspicion of latent lupus. The importance of arteriosclerosis is stressed by Gordon,⁸⁷ as a cause of seizures in the older age group. He found

convulsions beginning between the ages of 57 and 68 years, accompanied by episodes of vertigo and of focal pareses and due to cerebral vascular disease. Children with purulent meningitis have a grave prognosis when convulsive seizures occur in the course of the illness.⁷⁸ Convulsive seizures have again been reported⁶³ as a prominent part of the clinical picture of schistosomiasis. Following a prolonged course of EST, spontaneous grand mal seizures have been reported.¹⁰ The concurrence of epilepsy and tetany has been studied by Gotta³⁴ and he concludes they are separate entities even when concurrent, and that hypocalcemia may merely precipitate seizures in a patient who has a tendency to develop seizures. Anticonvulsant medication may, by controlling the seizures, obscure an underlying chronic hypoparathyroidism.⁹⁰

In this era of the extensive use of ACTH and similar preparations, it is noteworthy that convulsive seizures may be precipitated by the use of ACTH or cortisone¹⁸ and this is not dependent upon previous occurrence of seizures. The development of seizures is not related to disturbances of blood electrolytes and the convulsions may be followed by prolonged coma.⁸⁵ Antabuse therapy for abnormal drinking has been complicated by the appearance of seizures.⁸ Likewise the use of antihistaminic preparations¹⁰⁷ has precipitated seizures especially in children. Again seizures resulted from intrathecal penicillin.⁶⁵

This year has seen the reevaluation of the possible role of anoxia in the genesis of epilepsy. The similarity has been noted between the clinical pictures of anoxia and of epilepsy.^{23, 76} Nielsen⁷⁶ has shown epilepsy occurs twice as frequently in the first born as in other siblings and ascribes this to anoxia attendant upon the greater travail of the first birth. Doubt is cast, therefore, on the concept that the focal areas of cell loss in the epileptic cerebral cortex are the result of the anoxia of the seizures; it seems more probable that they are the result of the anoxia at birth. Along the same lines, though on less sure footing, Velasco⁹⁹ concludes that the hypoplasia and gliosis of Ammon's horn is important in the genesis of epilepsy. Harris⁹⁹ stressed the importance of cerebral hemorrhage as the cause of seizures in the first few days of life. This year, W. Lennox compiled his studies on heredity and added further studies on co-twins.⁵⁸ Seizures occurred in 3.2 per cent of the relatives of epileptics. The incidence was higher in the relatives of idiopathic epileptics (3.6 per cent) and lower in the relatives of post-traumatic epileptics (1.8 per cent). When a patient's seizures started later in life the incidence of seizures in relatives was less. The studies on twins revealed that when brain damage was not present and one twin had seizures, 84 per cent of the co-twins of one egg twins had seizures and only 22 per cent of the co-twins of two egg twins had convulsions. From this

data, Lennox concluded both brain damage and a transmitted predisposition to epilepsy are important in the genesis of epilepsy. Paroxysmal dysrhythmia is probably an indicator of the transmissible predisposition to epilepsy. The role of heredity is probably no greater here than in other diseases and it is important to consider each patient individually from the standpoint of marriage and procreation. The incidence of trauma prior to the development of seizures in children was found by Pine⁸⁴ to be as great as 32 per cent and he also noted that the onset of seizures was associated with fever in 10 per cent of his cases.

Interest this year has been great in the non-convulsive forms of epilepsy. Gibbs and Gibbs³¹ reported the constellation of rage, vegetative symptoms, and pain occurring in attacks in patients presenting 14 and 6 per second spiking discharges in EEGs taken during sleep. These discharges are of subcortical origin^{31, 94} and the clinical seizures can easily be confused with psychomotor epilepsy. Paroxysmal abdominal pain was again described as an epileptic manifestation.^{41, 64} Hoefer et al.⁴¹ presented 33 cases, thirty-one had abnormal EEGs; only nine also had convulsive seizures and postictal sleep was common after the attacks of pain. The attacks of abdominal pain may disappear in adolescence. The mechanism of the abdominal pain, in at least some cases, is intestinal intussusception.⁴¹ Matzilovich and Merlis⁷⁰ commented on the possibility of headache occurring as an epileptic manifestation. The headache is probably not a true aura but the cerebral dysrhythmia may lead to a sequence of events culminating in headache or head pain.

Petit mal seizures may occur in status⁹⁷ and the differential diagnosis is then difficult and electroencephalography is virtually mandatory to delineate the entity. The group of psychomotor seizures have been divided by Lennox⁶⁹ into a triad of psychomotor, automatic and psychic seizures with admixtures of types. Merlis and Golub³³ observed three phases of psychomotor seizures in the same patients. The first phase is one of suspended activity, the second one of stereotyped activity and in the third phase there are complex acts representing an interplay with environment. This demonstrates a complexity about psychomotor seizures which correlated well with experimental data from the Montreal group.^{49, 69} Psychomotor seizures have been reported due to chronic, bilateral and subdural hematomas.⁶¹ Seizures have been reported in tuberous sclerosis⁶² and in brain tumors.^{7, 94}

In the field of sensory precipitated epilepsy, Daly and Bickford¹⁵ reported photic-driven seizures occurring in twins, and Dow¹⁹ demonstrated by electroencephalography a temporal lobe focus in musico-genic epilepsy. Photic stimulation has also been reported to produce visual hallucinations⁷⁵ but the report is questionable since the phenomenon could not be repeated and the patient was also psychotic.

NEUROPHYSIOLOGIC FACTORS

Electroencephalography is reviewed in Chapter 13. A major contribution to neurophysiologic factors is the monograph by Penfield and Kristiansen⁸⁰ and it is impossible here to adequately review this great collection of data. Ingram⁴⁵ presented a concise resumé of cortical physiology in reference to seizures.

The most important controversy at this time concerns the site of origin of the electrical discharges producing psychomotor seizures. The evidence of Bailey and Gibbs⁴ pointed to a temporal lobe origin. Jasper and his co-workers^{48, 49, 69} indicated the importance of subcortical structures. Green and his colleagues³⁶ inclined toward the presence of both mechanisms. At the present state of our knowledge it appears that a strictly unilateral anterior temporal focus is of cortical origin and the bilateral anterior temporal lobe foci are of subcortical origin. The anatomic and physiologic basis for the subcortical potentialities have been determined by the Montreal investigators.^{48, 69} By methods of physiologic neuronography, the anterior temporal lobe has been shown to be in connection with the pulvinar of the thalamus, nucleus lateralis of the thalamus, the posterior complex of the thalamus, the central area of the thalamus, the hypothalamus, the basal ganglia and the thalamic reticular substance. Many of these connections are multisynaptic.

M. Lennox and F. Robinson⁵⁶ produced in experimental animals, by stimulation of the anterior cingulate gyrus, attacks resembling petit mal epilepsy. This indicates that the cingulate and cerebellar systems as well as the midline thalamic nuclei may be of importance in the genesis of petit mal epilepsy.

Interest in experimental seizures due to agenzized flour has waned considerably and there were only two reports in the literature this year.^{5, 55} A critical evaluation of acetylcholine²⁴ showed that this substance is a convulsant drug but is not an important factor in clinical epilepsy.

PSYCHOLOGIC AND SOCIAL FACTORS

Observations this year on intellectual and emotional problems of patients with epilepsy have been at variance. Zimmerman et al.¹⁰⁷ indicated a relationship between the degree of unconsciousness in seizures and the intelligence level of the patients, as patients with petit mal epilepsy show less intellectual impairment. However, Lennox⁵⁸ from his studies on twins concluded that brain damage and not the seizures is the important factor in impairment of intelligence. The Rorschach studies by Zimmerman¹⁰⁷ indicated "organicness" even in idiopathic epileptics. Winfield's¹⁰³ studies also showed that brain damage was an important factor in impairment of intellect.

The behavior problems of children have been the object of study by Bradley⁹ and Merritt.⁷³ The behavior difficulties in children may be the direct result of the neurophysiologic disturbance and, therefore, associated with the EEG changes and related to the seizures. On the other hand, they may merely represent the reaction of a sick child and his response to his particular environment. It is obviously important to consider the emotional and behavior reaction of epileptic children, as well as pharmacologic therapy. This is stressed by Berlin and Yeager⁶ who found the incidence of seizures may be dependent upon the emotional states of the parents. The results of group therapy in epileptics are reported by Randall and Rogers⁸⁶ who find group therapy as efficacious as individual therapy, especially in certain Latin American patients. In choosing patients for group therapy the pre-existing personality configurations are important. The social and family aspects of epilepsy were also stressed by Lennox⁵⁷ and Revitch⁸⁷ and MacQueen.⁶⁷ Peterson, Sumner and Jones³³ suggested the use of hypnosis in differentiating psychogenic from true seizures.

MEDICAL THERAPY

During this year, reports have appeared on several new drugs. Methylphenylsuccinimide (Milontin) was reported by Zimmerman¹⁰⁶ as particularly efficacious in the treatment of petit mal epilepsy. He stated it is equal to, or superior to, tridione and is less toxic. The average dose was 2.4 Gms. and the therapeutic dose was as high as 3.0 Gms. Ives⁴⁷ found Nuvarone useful but toxic, for it produced hemopoietic changes, itching and drowsiness. The pharmaceutical house which prepared Nuvarone has withdrawn it from experimental use. Stamps, Gibbs, and Haase⁹³ gave a preliminary report on the use of aureomycin in epilepsy. Other new drugs being tried experimentally include AC114, 1416L and Mysoline. At the present time there are no adequate reports on these preparations. Alphaphenylbutyryl urea was found to be efficacious in grand mal epilepsy but the toxicity was so great that studies were halted.⁷⁷ ACTH has been employed in six cases, four of whom were somewhat improved during the actual administration but following the cessation of therapy no lasting improvement occurred.⁵⁴ Desoxycorticosterone acetate was reported by Aird et al¹ as somewhat efficacious as an adjuvant to other anticonvulsant therapies. At the present time these endocrine preparations cannot be considered a treatment method of choice and there is little indication of any real assistance from them. Pyridoxine (Vitamin B6) has been conclusively labeled as ineffective from the anticonvulsant standpoint.¹⁴

Reviews of the present status of the standard anticonvulsants were numerous in the past year.^{2, 11, 25, 30, 81, 88, 91} The literature on mesantoin has been extensive.^{42-44, 50, 66, 80, 105} The general tenor of all these has been

cautious. The importance of the early signs of toxicity, weakness, drowsiness and malaise were stressed¹⁰⁵ for these may soon be followed by the symptoms due to bleeding tendencies. A newly reported complication of mesantoin therapy⁴⁴ is pigmentation of the skin due to melanin deposition.

Phenacemide (phenurone) was accepted this year by the Council on Pharmacy and Chemistry of the A.M.A. and is, therefore, a new and non-official remedy.¹³ The efficacy and toxicity of this drug have been considered extensively.^{17, 27, 51, 72, 81, 98} The most important review was that by Tyler and King⁹⁸ for it correlates most of the experimental work and presents the combined data on more than 1500 patients. Personality changes occurred in 17 per cent and usually within 4 to 6 weeks after the onset of phenurone therapy. Other toxic manifestations were changes in hematopoietic system, gastro-intestinal disturbances, rash, headache, drowsiness and insomnia. A careful selection should be made of the patients and phenurone should be used only when other standard preparations have failed to control seizures. Personality disorders and a history of allergic response to drugs are contraindications. During the time of therapy, observations should be made for evidences of liver damage or depression of bone marrow function. The patient or his family must be aware of the dangers of phenurone therapy. While the dose of phenurone usually varies from 1.5 to 3.0 Gms. Perry and Simons⁸² recommended a maximum dose of 2.0 Gms. P. Levin⁶⁰ suggested that phenurone may serve a particular function in the myoclonic seizures occurring in the rare, progressive encephalitides. At the present time, phenurone finds its greatest role in the treatment of psychomotor epilepsy but the prevailing opinion now is to employ dilantin, or dilantin and phenobarbital, as the mainstay of therapy and to employ phenurone if this method fails. Merlis⁷² stated that the usual procedure of studying monthly blood counts is of little value in preventing the fatalities due to the newer drugs. However, from the legal viewpoint, at least, it is unwise to abandon this safeguard.

The dangers of the new anticonvulsants have been forcibly demonstrated by Flaxman.²² Since 1946, there are in the literature 106 fatalities due to all drugs. Six of these reported cases are the results of new anticonvulsants and this is an incidence of 16 per cent. These figures are obviously not an accurate estimate of drug fatalities for, in the anticonvulsant field as in other fields, all fatalities are not reported. Nevertheless, the seriousness of this problem is quite obvious.

In the field of neuropharmacology, Chen¹² noted that in animal experiments electrically induced convulsions is the best method for evaluating possible drugs for treatment of grand mal seizures. The best anticonvulsant drugs for grand mal seizures have had a high anti-electric shock activity and no hypnosis. However, in some patients, a drug with slight sedative

action seems preferable. The anti-metrazol testing for evaluating drugs against petit mal epilepsy is questioned for carbromal is highly effective in this experimental set-up but is ineffective against clinical petit mal epilepsy. Toman⁹⁶ concluded from his studies that drugs effective against psychomotor seizures act to increase seizure thresholds and also to prevent the spread of seizure discharges. He also concluded that the success of phenurone in psychomotor epilepsy warrants the trial of other acetylureas.

Considerable interest has been evident this year in regard to the treatment of convulsions appearing in other diseases than epilepsy. Patients with seizures and lupus erythematosus should be treated with cortisone.⁸⁹ The patients who have both tetany and epilepsy should be treated with an eye to raising the blood calcium by the use of calciferol or dihydrotachysterol.³⁴ The occurrence of convulsions during acute purulent meningitis necessitates phenobarbital therapy,⁷⁸ and, in fact, children with purulent meningitis should be treated with phenobarbital as a preventive measure since the avoidance of seizures increases the recovery rate from 80 per cent to 96 per cent. Patients with severe allergic manifestations in addition to seizures should also be treated with anti-allergic medications.¹⁶

SURGICAL THERAPY

The conservative opinion in the general field of surgical therapy of focal epilepsy was expressed by Walker.¹⁰⁰ About 20 to 25 per cent of patients with focal epilepsy are candidates for surgical therapy. In general, medical therapy should be tried and found wanting before consideration of surgical therapy, unless the nature of the lesion is such as to render surgical intervention mandatory. Three types of surgical intervention are available, viz., subpial resection, lobectomy and hemispherectomy. The nature, location and extent of the lesion determines the choice of the procedure. Walker also recommended a five year period post-operatively before assessing the results of the extirpation. While the advances of electrocorticography have been great, the view of Guillaume, Mazars and Mazars³⁸ that it supersedes cortical electrostimulation is extreme.

The neurosurgical problems of psychomotor epilepsy have again held great interest. Bailey and Gibbs⁴ reported 25 cases of psychomotor epilepsy treated by radical excision of the temporal lobes. They, too, took a stand for conservative evaluation and pointed out the experimental nature of this procedure. Jasper, Pertuiset and Flanigin⁴⁰ reported 91 patients with temporal lobe seizures but less than half of their cases had psychomotor seizures. This incidence is concurred in by others.⁴⁶ Improvement was markedly lessened in unilateral temporal lobectomies if the patients had bilateral temporal lobe foci. Electrocorticography during psychomotor seizures showed suppression followed by high voltage 3 to 6 per second waves

and, after that, exhaustion. This evaluation of the temporal lobe focus is important for it shows that different mechanisms are at work during different phases of the psychomotor attack. The field of psychomotor seizures is, therefore, much more complicated than seemed evident at first and this correlates with the clinical observations of Golub and Merlis.³³

Green et al.,^{35, 36} in evaluating the role of surgery in psychomotor epilepsy, noted that anterior temporal lobectomy is effective in selected cases. The criteria of selection are (a) signs and symptoms of temporal lobe lesions, (b) incapacitating and medically refractory psychomotor seizures, (c) a minimal component of rage in the seizure pattern, and (d) a unilateral, temporal lobe focus by EEG. Definite contraindications to temporal lobectomy are rage reactions even if uncontrollable by medications, absence of evidence of a temporal lobe seizure, absence of focal temporal lobe EEG abnormality or the presence of a generalized EEG abnormality.

This year, then, has witnessed advances in the understanding of the role of surgery in the therapy of psychomotor epilepsy and underlined the fact that surgical treatment is still not an ordinary surgical procedure and should be relegated to capable hands and discriminating minds.

REFERENCES

- ¹ Aird, R. B. and Jordan, G. S.: Anticonvulsant properties of desoxycorticosterone. *J.A.M.A.* 145:715, 1951.
- ² Arieff, A. J.: Twelve year resume in a clinic for epilepsy. *Dis. Nerv. System.* 12:19, 1951.
- ³ Bailey, Pearce, Lennox, W. G., Merlis, J. K., and Walker, A. E.: Seizure—The Medical Treatment and Social Problems of Epilepsy. Veterans Administration film, 1951.
- ⁴ Bailey, Percival, and Gibbs, F. A.: A surgical treatment of psychomotor epilepsy. *J.A.M.A.* 145:365, 1951.
- ⁵ Belford, J. and Bonnycastle, D. P.: Biochemical changes observed during agene induced convulsions. *Arch. Neurol. & Psychiat.* 64:797, 1950.
- ⁶ Berlin, I. N. and Yeager, C. L.: Correlation of epileptic seizures, EEG and emotional state. *Am. J. Dis. Child.* 81:664, 1951.
- ⁷ Bormann, H. and Schiefer, W.: Krampfanfalle bei tumoren des grosshirns. *Deut. Zeitsch. Nervenheilk.* 166:1, 1951.
- ⁸ Bowman, K. M. et al.: Clinical evaluation of tetraethylthiuramides (antabuse) in treatment of problem drinkers. *Am. J. Psychiat.* 107:832, 1951.
- ⁹ Bradley, C.: Behavior disturbances in epileptic children. *J.A.M.A.* 146:437, 1951.
- ¹⁰ Browne-Mayers, A. N. and Henley, T. F.: Case report: grand mal convulsions following more than 150 EST. A clinical and EEG study. Read at meeting of Eastern EEG Soc., Dec. 16, 1951.
- ¹¹ Carter, S.: Use of anticonvulsant drugs. *GP.* 4:41, 1951.
- ¹² Chen, G., Ensor, C. R., and Clark, I. G.: Central nervous action of hydantoin, oxazolidinediones and thiozolidines. *Arch. Neurol. & Psychiat.* 66:329, 1951.
- ¹³ Council on Pharmacy and Chemistry, A.M.A.: *J.A.M.A.* 147:60, 1951.
- ¹⁴ —: *J.A.M.A.* 147:323, 1951.

- ¹⁵ Daly, D. and Bickford, R. G.: Electroencephalographic studies of identical twins with photo-epilepsy. *EEG Clin. Neurophysiol.* 3:245, 1951.
- ¹⁶ Dees, S. C. and Lowenbach, H.: Allergic epilepsy. *Ann. Allergy.* 9:446, 1951.
- ¹⁷ Dejong, R. N.: Phenurone in the treatment of psychomotor attacks. *Am. J. Psychiat.* 107:825, 1951.
- ¹⁸ Dorfman, A., Apter, N. F., Smull, K., Bergenstall, D. M., and Richter, R. B.: Status epilepticus coincident with use of adrenocorticotrophic hormone. Report of three cases. *J.A.M.A.* 146:25, 1951.
- ¹⁹ Dow, R. S.: Electroencephalographic findings in a case of musicogenic epilepsy. Exhibited at Meeting of American EEG Soc. 6:16-17, 1951.
- ²⁰ Editorial: Surgical treatment of focal epilepsy. *J.A.M.A.* 146:820, 1951.
- ²¹ Everett, G. M. and Toman, J. E. P.: Experimental "psychomotor" seizures and antiepileptic drugs. *Federation Proc.* 10:293, 1951.
- ²² Flaxman, N.: Drug fatalities. *J.A.M.A.* 147:377, 1951.
- ²³ Forster, E.: Vascular component in clinical picture of epilepsy. *Deutsche med. Wchnsch.* 76:732, 1951.
- ²⁴ Forster, F. M.: Critical evaluation of the possible role of acetylcholine in epilepsy. *J. Neuropath. & Clin. Neurology.* 1:98, 1951.
- ²⁵ —: Medical therapy of epilepsy. *Neurol.* 1:153, 1951.
- ²⁶ —: Seizure manifestations ipsilateral to cerebral lesion. *J. Neuropath. & Clin. Neurol.* 1:309, 1951.
- ²⁷ —: Therapy of psychomotor epilepsy. *J.A.M.A.* 145:211, 1951.
- ²⁸ Frankel, A. L. and Rothermich, N. O.: Polyarteritis nodosa: A review together with report of a case due to hydantoin sensitization treated with cortisone. *Ohio State M.J.* 47:1013, 1951.
- ²⁹ Funkhouser, J. B.: Psychiatric aspects of epilepsy. *West Virginia M.J.* 46:304, 1950.
- ³⁰ Garvin, J. S.: Medical treatment of epilepsy today. *Illinois M.J.* 98:344, 1950.
- ³¹ Gibbs, E. L. and Gibbs, F. A.: Electroencephalographic evidence of thalamic and hypothalamic epilepsy. *Neurol.* 1:136, 1951.
- ³² Gibbs, F. A.: Differential diagnosis and treatment of certain non-convulsive types of epilepsy. *Arch. Neurol. & Psychiat.* 65:403, 1951.
- ³³ Golub, L. M., Guhleman, H. V., and Merlis, J. K.: Seizure patterns in psychomotor epilepsy. *Dis. Nerv. System.* 12:73, 1951.
- ³⁴ Gotta, H.: Tetany and epilepsy. *Arch. Neurol. & Psychiat.* 66:714, 1951.
- ³⁵ Green, J. R., Duisberg, R. E. H., and McGrath, W. B.: Electroencephalography in psychomotor epilepsy. *EEG & Clin. Neurophysiol.* 3:293, 1951.
- ³⁶ —: Focal epilepsy of psychomotor type. *J. Neurosurg.* 8:157-172, 1951.
- ³⁷ Gordon, A.: Epilepsy in arteriosclerosis. *J. Nerv. & Ment. Dis.* 113:170, 1951.
- ³⁸ Guillaume, J., Mazars, G., and Mazars, Y.: Present status of surgical treatment of epilepsy. *Semaine d. hôp. Paris.* 27:871, 1951.
- ³⁹ Harris, L. E.: Emergencies in the newborn period. *Minnesota Med.* 33:1204, 1950.
- ⁴⁰ Higgins, J., Lederer, H., and Rosenbaum, M.: Life situations, emotions, and idiopathic epilepsy. *Research Publ., A. Nerv. & Ment. Dis.* 29:137, 1951.
- ⁴¹ Hoefler, P. F. A., Cohen, S. M., and Greeley, D. McL.: Paroxysmal abdominal pain. A form of epilepsy in children. *J.A.M.A.* 147:1, 1951.
- ⁴² Hofstatter, L.: Mesantoin in the management of the hospitalized psychotic epileptic. *South. M.J.* 44:827, 1951.
- ⁴³ Houfek, E. and Herrman, H. T.: Mesantoin in difficult cases of epilepsy. *Nebraska M.J.* 36:234, 1951.

- ⁴⁴ Hunter, H. and Jenkins, D.: Occurrence of skin pigmentation during mesantoin therapy. *J.A.M.A.* 147:744, 1951.
- ⁴⁵ Ingram, W. B.: A discussion of the neurological basis for seizures. *J. Iowa M. Soc.* 41:114, 1951.
- ⁴⁶ Iobst, C. W. and Forster, F. M.: Electroencephalographic foci in temporal lobes with consideration of seizure manifestations. *Neurology.* 1:309, 1951.
- ⁴⁷ Ives, E. R.: Comparison of efficacy of various drugs in treatment of epilepsy. *J.A.M.A.* 147:1332, 1951.
- ⁴⁸ Jasper, H. Marsan, C. A., and Stoll, J.: Corticofugal projections to the brain stem. *T. Am. Neurol. A.* 3-9, 1951.
- ⁴⁹ —, Pertuiset, B., and Flanigin, H.: EEG and cortical electrograms in patients with temporal lobe seizures. *Arch. Neurol. & Psychiat.* 65:272, 1951.
- ⁵⁰ Jones, D. P.: Methoin in treatment of epilepsy. *Brit. M.J.* 1:64, 1951.
- ⁵¹ Keith, H. M.: The use of phenurone in convulsive disorders of children. *Am. J. Dis. Child.* 89:719, 1950.
- ⁵² Kerschman, J., Vasquez, J., and Goldstein, S.: Incidence of focal and nonfocal abnormalities in the EEG. *EEG & Clin. Neurophysiol.* 3:15, 1951.
- ⁵³ Kimball, O. P.: A surgical approach to the control of epilepsy. *Ohio State M.J.* 47:842, 1951.
- ⁵⁴ Klein, R. and Livingston, F.: Effect of adrenocorticotrophic hormone in epilepsy. *J. Pediat.* 37:733, 1950.
- ⁵⁵ Laufer, W. W., Denhoff, E., and Giunta, F.: Clinical study in man of the effects of variation of aigenized flour products in the diet. *J. Pediat.* 38:341, 1951.
- ⁵⁶ Lennox, M. A. and Robinson, F.: Cingulate-cerebellar mechanisms in physiologic pathogenesis of epilepsy. *EEG & Clin. Neurophysiol.* 3:197, 1951.
- ⁵⁷ Lennox, W. G.: Epilepsy—a problem in public health. *Am. J. Pub. Health.* 41:533, 1951.
- ⁵⁸ —: Heredity of epilepsy as told by relatives and twins. *J.A.M.A.* 146:529, 1951.
- ⁵⁹ —: The psychomotor epilepsies. *J. Nerv. & Ment. Dis.* 114:81, 1951.
- ⁶⁰ Levin, P.: Read at meeting of Southern and Eastern EEG. Soc., 1951.
- ⁶¹ Levin, S.: Psychomotor epilepsy as a manifestation of subdural hematoma. *Am. J. Psychiat.* 107:501, 1951.
- ⁶² Lichtenstein, B. W. and Maslenka, S.: Epilepsy of organic origin. Report of a case. *Arch. Neurol. & Psychiat.* 66:389, 1951.
- ⁶³ — and Simon, A.: Cerebral schistosomiasis producing epilepsy in a veteran of the Pacific. *J. Neuropath. & Clin. Neurol.* 1:80, 1951.
- ⁶⁴ Livingston, S.: Abdominal pain as a manifestation of epilepsy (Abdominal epilepsy) in children. *J. Pediat.* 38:687, 1951.
- ⁶⁵ Lugli, G., Roberto, B., and Ruga, T.: Accessi epilettiformi nel corso del trattamento penicillinico per via endorachidia; considerazione sulla posologia e la tecnica del trattamento oto-rhino-larynx. *Ital.* 19:161, 1951.
- ⁶⁶ Littlejohn, W. S., Little, S. C., and McLallen, C. D.: Mesantoin in the treatment of convulsive disorders. *Dis. Nerv. System.* 12:269, 1951.
- ⁶⁷ MacQueen, J. C.: The medical care of children with paroxysmal convulsive disorders. *J. Iowa M. Soc.* 41:111, 1951.
- ⁶⁸ Mallin, A. W. and Gammon, G. D.: Clinical evaluation of Mesantoin in treatment of epilepsy. *Arch. Neurol. & Psychiat.* 65:128, 1951.
- ⁶⁹ Marsan, C. A. and Stoll, J.: Subcortical connections of the temporal lobe in relation to temporal lobe seizures. *Arch. Neurol. & Psychiat.* 66:669, 1951.

- ⁷⁰ Matzilivich, B. and Merlis, J. K.: Headache as an epileptic manifestation. *Arch. Neurol. & Psychiat.* 66:651, 1951.
- ⁷¹ Merlis, J. K., Grossman, C., and Henriksen, G. F.: Comparative effectiveness of sleep and metrazol activated EEGs. *EEG & Clin. Neurophysiol.* 3:71, 1951.
- ⁷² —: Medical treatment of psychomotor epilepsy. *Neurology.* 1:245, 1951.
- ⁷³ Merritt, H. H.: Anti-epileptic drugs in the treatment of behavior disorders. Research Publ., A. Nerv. & Ment. Dis. In press.
- ⁷⁴ Myers, R.: Neurosurgical measures in the management of "epilepsy." *J. Iowa M. Soc.* 41:128, 1951.
- ⁷⁵ Mundy-Castle, A. C.: A case in which visual hallucinations related to past experience were evoked by photic stimulation. *EEG. Clin. Neurophysiol.* 3:353, 1951.
- ⁷⁶ Nielsen, J. M. and Courville, C. B.: Role of birth injury and asphyxia in epilepsy. *Neurology.* 1:48, 1951.
- ⁷⁷ Orloff, M. J. et al.: Anticonvulsant and toxic effects of alaphabutylurea. *Neurol.* 1:377, 1951.
- ⁷⁸ Ounsted, C.: Significance of convulsions in children with purulent meningitis. *Lancet.* 1:1245, 1951.
- ⁷⁹ Penfield, W. and Gerber, W. F.: Observations on epileptic patterns and the supra-cortical integrating system. Research Publ., A Nerv. & Ment. Dis. In press.
- ⁸⁰ — and Kristiansen, K.: Epileptic Seizure Patterns. A study of the localizing value of initial phenomena in focal cortical seizure. Illinois, Charles C Thomas, 1951.
- ⁸¹ Perlstein, M. A.: Newer drugs in the therapy of epilepsy. *Illinois M.J.* 99:75, 1951.
- ⁸² Perry, G. F. and Simons, S.: Phenacetylurea in the convulsive disorders. *Dis. Nerv. System.* 12:200, 1951.
- ⁸³ Peterson, D. B., Sumner, J. W., and Jones, G. A.: Role of hypnosis in differentiation of epileptic from convulsive-like seizures. *Am. J. Psychiat.* 107:428, 1950.
- ⁸⁴ Pine, I., Reynolds, D. H., and O'Rear, H. B.: Convulsive disorders in children. A study of the Duke Hospital Pediatric Convulsive Clinic. *North Carolina M.J.* 12:129, 1951.
- ⁸⁵ —, Engel, F. L., and Schwartz, T. B.: Electroencephalogram and ACTH and cortisone treated patients. *EEG & Clin. Neurophysiol.* 3:301, 1951.
- ⁸⁶ Randall, G. C. and Rogers, W. C.: Group therapy for epileptics. *Am. J. Psychiat.* 107:422, 1950.
- ⁸⁷ Revitch, E.: Social aspect of epilepsy. *J. M. Soc. New Jersey.* 48:100, 1951.
- ⁸⁸ Ruskin, D. B.: Comparative results in seizure control using phenobarbital, dilantin, and mesantoin. *Am. J. Psychiat.* 107:415, 1950.
- ⁸⁹ Russell, P. W., Hasserick, J. R., and Zucker, E. M.: Epilepsy in systemic lupus erythematosus. *Arch. Int. Med.* 88:78, 1951.
- ⁹⁰ Schottstaedt, W., Gordon, G. S.: Chronic idiopathic hypoparathyroidism stimulating epilepsy. *California Med.* 74:390-391, 1951.
- ⁹¹ Schuler, F. W. and Featherstone, R. L.: A brief survey of the pharmacology of antiepileptic drugs. *J. Iowa M. Soc.* 41:125-128, 1951.
- ⁹² Schwab, R. S.: *Electroencephalography in Clinical Practice.* Philadelphia, W. B. Saunders, 1951.
- ⁹³ Stamps, F. W., Gibbs, E. L., and Haase, E.: Epileptic patients treated with aureomycin. *Dis. Nerv. System.* 12:227, 1951.
- ⁹⁴ Stephenson, W. A.: Intracranial neoplasm associated with 14 and 6 per second positive spikes. *Neurology.* 1:372, 1951.

- ⁹⁵ Tichner, J. B. and Enselberg, C. D.: Suicidal dilantin (sodium diphenylhydantoin) poisoning. *New England J. Med.* **245**:723, 1951.
- ⁹⁶ Toman, J. E. P.: Neuropharmacologic consideration of psychic seizures. *Neurology*. **1**:444, 1951.
- ⁹⁷ Tucker, W. and Forster, F. M.: Petit mal epilepsy occurring in status. *Arch. Neurol. & Psychiat.* **64**:823, 1950.
- ⁹⁸ Tyler, M. W. and King, E. Q.: Phenacemide in treatment of epilepsy. *J.A.M.A.* **147**:17, 1951.
- ⁹⁹ Velasco, O. P.: Contribucao anatomica-clinica as atuais concepcoes sobre a epilepsia. *Arq. neuro-psiquiat.*, São Paulo. **8**:301, 1950.
- ¹⁰⁰ Walker, A. E.: Treatment of cortical epilepsy by cortical excision. *J. Pediat.* **38**:285, 1951.
- ¹⁰¹ Watson, C. W.: Review of psychiatric progress, 1950; epilepsy. *Am. J. Psychiat.* **107**:535, 1951.
- ¹⁰² Weingarden, J. B. and Seever, M. H.: Toxic effects of antihistaminic drugs. *J.A.M.A.* **105**: 257, 1951.
- ¹⁰³ Winfield, D. L.: Intellectual performance of cryptogenic epileptics, symptomatic epileptics, and post traumatic encephalopathies. *J. Abnorm. & Social Psychol.* **46**:336, 1951.
- ¹⁰⁴ Winkler, E. G., Freiman, G. V., and Lieberman, S. S.: Astrocytoma of left temporal lobe. Contribution to the problem psychopathology or epileptic personality disorder and to the problem of semantic aphasia. *Am. J. Psychiat.* **108**:343, 1951.
- ¹⁰⁵ Witkins, E. and Waide, M.: Aphasia of bone marrow during mesantoin therapy. Report of a fatal case. *J.A.M.A.* **147**:757, 1951.
- ¹⁰⁶ Zimmerman, F. T.: The use of methylphenylsuccinimide in treatment of petit mal epilepsy. *Arch. Neurol. & Psychiat.* **66**:156, 1951.
- ¹⁰⁷ —, Burgemeister, B. B., and Putnam, T. J.: Intellectual and emotional makeup of the epileptic. *Arch. Neurol. & Psychiat.* **65**:545, 1951.

The Autonomic Nervous System

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ANATOMY

CENTRAL AUTONOMIC MECHANISMS. Anatomic data relative to the relationships of the hypophysis and the hypothalamus in normal man,³³⁸ and in a microcephalic idiot,³⁵⁴ and alterations in the hypothalamus following almost complete destruction of the hypophysis in a male and following castration in a female,³⁴⁵ have been reported. Experimental data obtained from rats indicate the existence of a localized feeding center in the hypothalamus.⁶ An emetic chemoreceptor trigger zone is located in the medulla oblongata between the ala cinerea and the vestibular nuclei.²⁸ The assumption that expiratory and inspiratory reactions are mediated through distinct but closely associated centers in the medulla oblongata is supported by additional data.²⁵⁵ Other data support the assumption that the respiratory center is located at the level of the medullary striae in the floor of the fourth ventricle.¹³⁷ Neoformation of neurons of the preganglionic type in the cervical spinal cord of chick embryos transplanted into the thoracic region has been described.²⁷³ Cell proliferation in the ependymal layer in the hypothalamus has been observed in the hamster three to five days after birth.¹³

The central pathways for visceral afferent impulses conducted through the splanchnic nerves are located in the dorsal and the lateral funiculi in the spinal cord. Those for speeds of 22 to 36 meters per second lie in the ipsilateral funiculus and lead to the nucleus gracilis. From this level the impulses are conducted through the contralateral medial lemniscus. Those for conduction rates of six to ten meters per second are located bilaterally in the region of the spinothalamic tracts. They lead to the hypothalamus and the caudal portion of the thalamus bilaterally.¹⁰²

Preganglionic Outflow. In the frog, fine myelinated nerve fibers, presumably preganglionic, have been observed in all the ventral spinal nerve roots from the 1st to the 8th inclusive.²⁴⁴ Preganglionic pupillodilator fibers have been demonstrated in the communicating rami that join the 3rd, the 4th and the 5th sympathetic trunk ganglia.¹⁶⁸ The autonomic nervous

system in the chimeroid fish, *Hydrolagus collieri*, is essentially similar to that in the frog, *Rana pipiens*.²¹⁸

In the cat, the preganglionic fibers concerned with bronchodilatation emerge in the rostral few segments of the sympathetic outflow.⁵⁷ The communicating rami and the sympathetic roots in the lumbar segments and the lumbar portion of the sympathetic trunk in the dog have been analyzed in detail.²⁰⁷ The variability in the anatomic relationships and the number of the communicating rami and the sympathetic trunk ganglia in the lumbar segments previously demonstrated in man has been corroborated in human dissections.^{85, 329} On the basis of 100 human dissections, the splanchnic nerves appear to be made up of many rami, some of which are very minute, that arise from the sympathetic trunk from the 6th thoracic to the 1st lumbar ganglia.²⁵² The courses of the visceral rami of the sacral nerves to the urinary bladder have been traced in human fetuses.¹⁶⁰ In dogs and cats, the preganglionic fibers to the adrenal medulla traverse the ventral roots of the 7th, the 8th, and the 9th thoracic nerves. The sympathetic and the sensory fibers distributed to the adrenal cortex traverse the 9th, the 10th, and the 11th thoracic nerves.¹⁶³ The sole origin from the Edinger-Westphal nucleus of preganglionic fibers to the ciliary ganglion has been confirmed in ducks and turkeys.²⁹³ Fibers of the hypothalamico-hypophyseal tract terminate most frequently in arborizations around blood vessels in the pars nervosa of the hypophysis. Some enter the pars intermedia and the pars tuberalis.¹⁰⁸

Autonomic Ganglia. The ganglion cells associated with the nervus terminalis in the rabbit have been described as solely autonomic.⁶⁹ This conclusion is at variance with certain earlier data. A plexus lying just above the nervus terminalis in the falx cerebri in man includes some small ganglia and appears to be related to the anterior ethmoid nerve.²⁷⁶

Pigment granules in the process of formation, fatty granules of two types, mitochondria, chromidia and the Golgi apparatus have been recognized in Sudan black preparations of mature sympathetic ganglion cells of the rabbit by use of the Zernike Microscope.⁹⁹ The ganglion cells are polarized, the axonal end being anterior. The Golgi apparatus is situated toward the anterior pole. Its broken down parts give rise to pigment. Pigment that is resistant to fat solvents may, nevertheless, be stained with Sudan black. Age appears to be a factor in the conditions of the ganglion cells. Certain aggregates of granules in human ganglion cells in subjects sixty years of age or older have been designated "senility pigment." They probably contain some form of neurosecretion.¹⁰⁰

The assumption that sympathetic ganglion cells may exhibit neurosecretory activity appears to be supported.^{84, 208} Amitotic nuclear division that results in binuclear ganglion cells has been observed in the rabbit.¹²⁰ In

man, binuclear ganglion cells have been found to be most abundant in the stellate and the 3rd lumbar sympathetic trunk ganglia.¹²⁴ Small, medium sized and large ganglion cells occur in varying proportions in different ganglia.

Preparations of sympathetic ganglia removed surgically from hypertensive patients exhibit chromatolysis in some ganglion cells, hyperchromatism of the nucleus in some, variable degrees of ganglion cell pigmentation and proliferation of capsule cells.²⁹⁸ None of these alterations can be regarded as indicative of hypertension. Preparations of ganglia from hypertensive dogs exhibit ganglion cells poor in chromidial substance in much larger numbers than preparations of ganglia from normal dogs.²¹⁵

Section of the preganglionic fibers to the ciliary ganglion in birds resulted in reduction in the size of the ganglion cells and hypertrophy and possible hyperplasia of the supporting cells. A reduction in the number of ganglion cells became apparent 90 days after preganglionic section. After regeneration of the preganglionic fibers, the surviving ganglion cells showed complete restoration.²⁹³ Structural alterations of synaptic endings in human sympathetic ganglia have been described.⁶¹ Most of the alterations observed in human sympathetic trunk ganglia that are causally related to disease appear to be reversible.⁸⁶

Chromaffin tissue has been observed in thoracic and lumbar sympathetic trunk ganglia²⁹⁷ and in association with the nodose ganglion³¹² in man. Chromophobe cells that are regarded as of neural origin have been observed in the human skin.²²¹ Small ganglia have been observed in the region of the cavernous sinus and in the oculomotor and the maxillary nerves in the rabbit.¹⁰¹

Cardiac Nerves. In the mouse, the cardiac ganglia lie chiefly in the sub-epicardial tissue. On the basis of their distribution, they have been designated as supracardiac and atrial.²²² The extrinsic cardiac nerves, except some sympathetic rami, enter the ganglia directly. In the dog, the cardiac ganglia appear to be concentrated at the base of the heart, but intramural ganglia have been observed in the right ventricle. Sympathetic and parasympathetic nerve fibers occur in the atria, the ventricles and the atrioventricular node. Afferent nerve fiber terminations were observed chiefly in the atria and the atrioventricular node.^{291, 292} In the calf's heart, tactile organs have been observed in the endocardium and the atrioventricular bundle.¹⁷⁸ A nerve plexus, probably sensory, on the ventricular surface of the pulmonary semilunar valves has been described in the guinea pig.¹⁸³ The atrioventricular bundle appears to be abundantly innervated in various mammals.⁹²

Enteric Plexuses. Argentophile and argentophobe ganglion cells have been described in the enteric ganglia in the mouse. Preganglionic vagus nerve

fibers make synaptic connections only with argentophile ganglion cells. The argentophobe ganglion cells are synaptically related to argentophile cells.¹³³ Chemical differences in the nerve fibers have also been considered.⁵² The occurrence of ganglion cells of the three types of Dogiel is corroborated.¹¹⁰ Certain data have been interpreted as supporting the assumption that the ganglion cells of Dogiel's type I are not motor, but associational, and that those of Dogiel's type II form part of a terminal syncytium that is superimposed on the ground plexus of Boeke.¹⁴¹⁻¹⁴⁴ The latter structure has been discussed further in relation to the terminal reticulum of Stöhr.²⁷ Alterations in the neuro-vascular system in the intestinal wall in patients with chronic obstipation have been described.²²⁸ Additional data have been reported relative to the absence of ganglion cells in the myenteric plexus in a zone near the distal end of the large intestine in patients with congenital megacolon.²⁶ The absence of ganglia in the submucous plexus in some amphibia has been noted.¹¹² Sensory nerve fiber terminations have been described in the human esophagus.¹⁸⁴

Innervation of Blood Vessels. In the cat, the innervation of the subepidermal vascular plexus appears to be chiefly sensory. In the vessels that supply skeletal muscles the sympathetic nerves lie close to the media. The sensory fibers form a plexiform structure in the adventitia.²⁴⁵ Further data relative to the sensory innervation of the vessels in the pachymeninges have been reported.²³⁷ In the cat, some intracranial vascular nerves have been traced directly from cranial nerve roots.⁴⁵ Additional data have been reported relative to afferent spinal nerve fibers that reach blood vessels in the extremities via the sympathetic trunk.¹⁷⁵ Data relative to the innervation of arterio-venous anastomoses have been reported.²⁰² Rami of the femoral nerve trunk that supply the deep and the superficial blood vessels of the limb have been described in rhesus monkeys and in human fetuses.³¹⁵

Innervation of the Urogenital Organs. Some new data relative to the distribution of nerve fibers in the kidney support the assumption that the renal tubules are directly innervated.²¹⁰ Other data fail to support this assumption.⁴⁶ New data relative to the innervation of the urinary bladder²⁴² and the uterus²⁴⁹ in general corroborate earlier findings. In mice, rats and rabbits, the ovarian nerves accompany the ovarian blood vessels.¹²⁹ Nerve fibers have been observed in proximity to the ovarian follicles,¹⁶⁴ in the membrana granulosa and in the corpus luteum,¹⁷² but a functional innervation of the follicles and the corpus luteum has not been demonstrated.

Miscellaneous. Data relative to the location and the form of the inferior cervical sympathetic ganglion in the human fetus have been reported.²¹³ Additional data relative to the occurrence and the distribution of accessory sympathetic ganglia, particularly in fetal monkeys, have been reported.³²² The assumption that the membranous labyrinth receives autonomic nerve

fibers is supported.²³⁵ Autonomic nerve fibers have been described in the substantia propria of the cornea. They probably are concerned with regulation of the flow of lymph in the fluid canaliculi.²⁶⁰ A terminal neural plexiform structure has been described in the respiratory bronchioles, the alveolar ducts and the alveoli in the lungs.¹⁸¹ Additional data relative to sympathetic conduction pathways that are independent of the sympathetic trunk confirm earlier findings.⁸³ Differential silver impregnation of autonomic nerve fibers appears to depend on the animal species used, the stage of development and the technique.³²¹ The surgical importance of the anatomic relationships of the nerves to the rectum and the plexiform structure around it has been pointed out.¹⁰⁵ In the magnocellular nuclei of the hypothalamus of the rat alkaline phosphatase activity was observed chiefly in capillaries and acid phosphatase activity chiefly in the nuclei and the cytoplasm of the neurons.⁸⁷ Parenteral administration of vitamin B₁₂ resulted in an increase in the pentose nucleic acid content, but in no appreciable change in the desoxypentose nucleic acid content in the sympathetic ganglion cells in young rats.³ Neurosecretory granules associated with the terminal neural structures in the neurohypophysis have been reported.^{24, 346} All the nerve fibers in the neurohypophysis appear to be of central origin. Their neurosecretory activity appears to be concerned with the production of the anti-diuretic hormone. The vascular bed at the adenoneurohypophyseal surface probably subserves chemoreceptive functions.³⁵¹ Ganglion cells of a peculiar type have been described in the hypophysis of *Rhodeus amarus*.³³⁹ The pars nervosa of the hypophysis in fishes and amphibians has been described as a collection of axonal terminals that store and release hormones produced by the cells of origin in the hypothalamus.³⁵⁰

PHYSIOLOGY

General. The harmonious working of the two divisions of the autonomic nervous system constitutes a demonstration of organic order.^{127, 132} Regulatory control originates in the diencephalon and the frontal cortex. Earlier data relative to autonomic responses to electrical stimulation of various cortical areas, particularly the rostral portion of the cingulate gyrus, the postorbital, the anterior insular, the anterior hippocampal and adjacent temporal cortical areas in the monkey and homologous areas in the cat and the dog have been confirmed and extended.¹⁵⁵ Stimulation of points in the amygdaloid and the caudate nuclei also results in lowering of blood pressure. Extensive review of the literature pertaining to the autonomic nervous system in allergic disease supports a theory of allergy based on autonomic vascular reactions.^{316, 317} This theory appears to be more consistent with clinical data than is the antigen-antibody concept.

The intake of food and of water is influenced by hypothalamic mecha-

nisms that tend to prevent plethora of stored fat or a deficit of body water.³⁵ Hypothalamic lesions produce hyperphagia in rats. This is normally inhibited by a hypothalamic satiety mechanism sensitive to changes in the blood brought about by ingestion of food.¹⁵⁸ Modifications of hypothalamic control of energy intake may be a prerequisite to obesity. The production of thyrotropin in the hypophysis is impaired by localized hypothalamic lesions in the suprachiasmatic and the caudal ventromedial nuclei.¹⁰⁹ The pars nervosa of the hypophysis is described as a collection of axonal terminals that stores and releases hormones synthesized by the neurons in the hypothalamus from which the axons arise.³³¹ The hypothesis that activation of the anterior lobe of the hypophysis is effected by a humoral mechanism is supported.³²⁷

In feeble minded children, ultrasonic stimulation of autonomic centers in the brain stem has no effect on pulse and blood pressure, but respiration, blood sugar and leucocyte count are increased.¹²² Leukotomy also results in autonomic disturbances.^{97, 247}

The effects of pharmacologic agents on autonomic ganglia are described, 171, 191, 194-196, 299 and adrenergic nerve mediators are considered.^{304, 305} Noradrenin normally controls the circulation while adrenin produces various effects during emergency. The order in which autonomic reflexes are abolished by anesthesia is determined by the natural impulse frequency of the reflex arcs.²⁶⁹

The chemoreceptor reflex mechanisms are outlined and their structure and function described.⁶⁵ Under conditions of hypoxia, increased discharges from the chemoreceptors may be elicited by reduction in the flow of blood through the glomus tissue and by reduction in the oxygen content of the blood flowing through this tissue.²¹⁶ Radiopaque material in the internal carotid artery in man elicited dilatation of the pupil and flushing of the face. These reactions were not elicited by injection of the same material in the external carotid artery.¹²¹ In ruminants, the chemical mediators liberated by vagus stimulation are not identical at the level of the heart and at the level of the stomach.³⁶ Fatigue of the light reflex mechanism appears to be accompanied by a shift in the autonomic functional balance.¹⁸⁶ The apparent contraction of the superior oblique muscle in the cat and the dog in response to cervical sympathetic stimulation appears to be due to traction on the muscle by other orbital structures such as the nictitating membrane.³⁴ In the rabbit, autonomic regulation of intraocular pressure has been demonstrated.⁶² Data relative to respiratory and vasomotor responses to afferent vagus stimulation have been reported.³⁴⁴

Circulatory System. The autonomic nervous system plays a part in regulating the contents of the blood.^{66, 177, 230, 294, 306} The number of leucocytes in the peripheral blood and the number of megakaryocytes in the bone

marrow is increased during sympathetic paralysis. Vagus paralysis results in a small increase in leucocytes with a marked decrease in erythrocytes. Stimulation of the posterior region of the tuber cinereum or the mammillary body in rabbits produces lymphopenia.

Vasodilatation in skeletal muscles can be caused by hypothalamic stimulation in a zone running from the rostral margin of the supraoptic area to the mammillary body.⁸⁵ Hypoxia directly affects the vasomotor centers in the central nervous system.¹⁷ Excitation is caused by a decreased blood flow and depression by an increased blood flow. The activity of the centers at any stage of hypoxia reflects the algebraic sum of the opposing influences. Intrapulmonary administration of CO₂ causes vasoconstriction of central or reflex origin in the intestine isolated *in situ*. This reaction probably is not physiologically significant.³⁴³ Vasoconstrictor centers are found in the medulla of the dog's spinal cord primarily in segments giving rise to the splanchnic nerves.⁴⁷ The hyperalgesic zones of Head appear to depend on the vascular pattern at the surface of the body and the organization of the peripheral sympathetic nerves.³³⁷

Changes in blood pressure have been observed due to cortical stimulation in the posterior orbital, the anterior insular and the cingulate areas and a limited area of the temporal lobe. The responses elicited from the posterior orbital and the insular cortex are abolished by destruction of the hypothalamus. Those due to stimulation in the other cortical areas referred to appear to be independent of the hypothalamus.³⁰⁸

Sympathetic activity is to a great extent responsible for control of the blood pressure level, and it is relatively independent of the available quantity of blood so long as a sufficient volume is present.¹¹³ In general, stimulation adequate to produce pain results in sympathetic discharge and resultant changes in blood pressure, but in cats and rabbits, these changes appear to be dependent upon perception of the pain.^{106, 107} In persons exhibiting autonomic dystonia peripheral stimulation of the stellate ganglion influences the capillary blood circulation in the edge of the fingernails and the blood sugar level, but central stimulation of the hypophysis and the diencephalon has no such effect.³²

Contrary to positive results of some previous workers, activation of parasympathetic vasodilator fibers supplying the intestine during depressor reflexes from the pressoreceptor regions is not demonstrated in the cat.⁴⁰ The vasodilatation seems to be effected solely by inhibition of constrictor tonus. Right vagus stimulation tends to produce ischemia in the gastric mucosa due to its influence on arterio-venous shunts. This may be a factor in ulcer formation.³³⁰ The blood pressure waves commonly known as Traube-Hering or vasomotor waves appear to be regulated by the pressoreceptor autonomic reflex system.^{114, 115} Indirect heating and tetraethyl-

ammonium bromide allow dilatation of the collateral vessels and increased blood flow in man during acute occlusion of the femoral artery.²⁷² Closure of the carotid arteries in cats causes splenic contraction due to a reflex mediated through splenic nerves.⁷⁵ In patients with hyperhydrosis and Raynaud's disease, sympathectomy results in no marked change in arterial pressure, but the flow of blood through the forearm is increased three-fold during the first three to four postoperative days.³³³

The arterio-venous anastomoses in the extremities of the dog are dilated by acetylcholine whereas the capillaries are constricted, but histamine dilates the capillaries and constricts the anastomoses. Adrenin constricts both.²⁶⁸ The significance of the anastomoses and the capillaries is discussed. The capillaries alone are responsible for the increased temperature of the ear of the rabbit during external heating.³⁰¹ When the blood vessels of the rabbit's ear are denervated, the reactions are more gradual and more responsive to adrenin.³⁰² Data have been advanced that appear to support the hypothesis that the superficial heat receptors are concerned with vascular readjustments and that deeper ones are concerned with sweating. The latter are readily stimulated by heat produced in working muscles. The apparent relationship of sweating to skin temperature is due to a temperature gradient between the arterial and the venous blood.¹⁵

Sympathetic nerve stimulation causes constriction of vessels in the rabbit's ear and increased critical closing pressure.¹⁰⁸ In hypertension associated with increased sympathetic activity the increase in blood pressure probably is necessary because of the increased closing pressure. After cardiac sympathectomy has abolished cardioacceleration chronic experimental neurogenic hypertension in dogs will endure to a considerable degree.²⁰⁶ Rapid heart rate and increased cardiac output, therefore, do not seem to be primary mechanisms. Acetylcholine hypertension in atropinized dogs is primarily due to stimulation of the aortic and the carotid sinus chemoreceptors, but with greater doses the vasomotor and the adrenal synapses are stimulated directly.¹²

The cause of depression of the vasodilator reflexes during hypertension is localized in the kidney-suprarenal-aortic zone.¹⁹⁰ The ganglia of the celiac plexus will not maintain the reflex. Acute occlusion of a normal artery in an extremity in man is followed within one minute by decreased collateral resistance. The decrease in collateral resistance caused by sympathectomy is transient in many cases.⁷² Stimulation of the distal portion of the divided hepatic nerves causes constriction of the intrahepatic branches of the portal vein and a rise in portal blood pressure.⁶⁰ Electrocardiographic effects of vagal stimulation have been analyzed.³⁴⁸

Digestive System. In the rat, the autonomic innervation of the incisors

and the adjacent tissues exerts no regulatory influence upon the rate of eruption even when fairly large changes in blood flow are produced.²⁸⁸

In man, secretion of gastric mucoprotein is completely suppressed following bilateral vagotomy, and concentration of mucoproteose is increased.¹⁰⁴ This indicates a rapid unfavorable degradation. Bilateral supradiaphragmatic resection of the vagi and extirpation of the pyloric antrum of the dog, however, are said to suppress gastric secretion and prevent development of stomal ulcers.²⁹⁹ The effects of vagotomy on the dog's stomach still persisted two years after operation.⁶³

In the cephalic phase of gastric secretion a combined neurohumoral mechanism appears to operate.¹⁸² Vagus stimulation probably activates the peptic cells, and gastrin may exert an effect by the release of histamine. Vagal stimulation results in the liberation of very little gastrin or none at all.^{147, 181}

Sympathectomy of the stomach results in an increase in gastric secretion suggesting that the sympathetic nerves are inhibitory.^{226, 270} The gastric motility and secretion resulting from ultrasonic stimulation applied at the 6th to the 9th thoracic segments in man is also thought to be due to inhibition of sympathetic nerve activity.¹³⁰

The myenteric plexus includes ganglion cells of two types that are functionally distinct.⁵ The axons of the one type are cholinergic and cause contraction of the gastro-intestinal musculature whereas those of the other type are adrenergic and mediate inhibition.

Muscular exertion influences the inhibitory action of adrenin on the musculature of the intestine,¹²⁵ and painful stimuli result in marked slowing of the propulsion of charcoal in the small intestine of the albino rat.³⁰³ The hooded rat is not affected in this way as it is more closely related to the wild type and probably less sensitive to pain.

When two balloons are placed five centimeters apart in the dog's duodenum and 2 cc. of N/10 HCl, 2 per cent soap or bile is injected between them, an increase in tonus and amplitude of duodenal contraction is indicated by the upper balloon and an opposite effect is indicated by the lower one.²⁹⁵ Removal of the myenteric plexus with the outer layer of the colon in cats and dogs from zones 1 to 6 cm. in length and 6 to 8 cm. proximal to the pelvic peritoneal reflection does not materially alter the size or the frequency of stools.¹⁶⁶ The interactions of diencephalic, emotional and hormonal influences on pancreatic, gastric and biliary functions are discussed.²⁶⁴

Respiratory System. Different kinds of atelectasis patterns during intra-thoracic operations suggest the neural character of the respiratory reactions, and the lungs seem to participate actively in respiration.²²⁰ The effects of vagal block indicate that pulmonary vagal fibers are chiefly excitatory on

inspiration,³⁰ but the effect of vagal stimulation on the bulbar respiratory center seems to be only inhibitory.⁷⁰ It may be significant in this regard that a ventro-medial inspiratory area and a dorso-lateral expiratory area are found in the bulbar part of the medulla oblongata in the rabbit.³¹⁹

The importance of chemoreceptors in the regulation of respiration is emphasized,¹²⁸ and it is shown that stimulation of the pressoreceptor and chemoreceptor areas results in reflex increase respectively of vagal and sympathetic tonus in the bronchi.⁵⁸ Bronchospasm in man, however, persists even after bilateral vagus section; and there are no gross changes in quantity or consistency of secretion.¹⁶⁵ In dogs and cats, electrical stimulation of the carotid sinus nerve causes bronchoconstriction or bronchodilatation. The bronchodilator response is diminished, abolished or reversed by section of the sympathetic nerves to the respiratory tract.⁵⁹

Urinary System. Electrical stimulation of foci on the anterior sigmoid gyri of cats produces renal cortical ischemia, but renal denervation essentially abolishes the reaction. After nineteen or more stimulations, the kidney changes suggested lower nephron nephrosis.¹³¹ Direct stimulation of renal nerves effects random closing of nephrons in dogs and constriction of vessels sufficient to cause temporary cessation of blood flow.¹³⁶ Evidence of vascular shunts, however, is not found.

The ability of the dog's kidney to excrete sodium and chloride during loading with mannitol in the hydropenic state is dependent on an intact sympathetic nerve supply,¹⁵⁶ and it is important to note that the sympathetic synapses concerned with the kidney and adrenal gland of the dog are located in the celiac plexus while those for the spleen are situated in the paravertebral ganglia.¹⁹²

Following unilateral pelvic nerve section no structural or functional changes are observed in the urinary bladder of the cat, but section of both pelvic nerves is followed by complete urinary retention for about ten days and by bladder hypertrophy.^{38, 39} In the absence of parasympathetic innervation, the bladder in the female dog rapidly becomes hypertonic.⁷⁹ The sympathetic fibers apparently play no significant role in accommodation or tonus of the bladder.

Distension of the bladder in man produces a bilateral pallor of the skin in the 11th and the 12th thoracic segments, but sympathectomy of these segments abolishes this effect.¹ Attempts to elicit purely sympathetic and purely parasympathetic bladder responses by electrical stimulation of selected areas in the forebrain have yielded no significant results.¹³⁸

Reproductive System. Localized lesions in the supraoptic and the tuberal areas of the rabbit's hypothalamus result in a marked numerical decrease of secretory cells in the oviduct, but the ciliated cells are unaffected.⁹⁴ It is

also shown that parturition proceeds more rapidly after sympathectomy of the uterus.¹⁴

Endocrine System. Centripetal vagus stimulation in dogs pithed below the 6th cervical segment liberates into the blood stream a vasopressor substance distinct from adrenin, noradrenin, renin, angiotoxin or pitressin; consequently, the brain appears to act as an endocrine organ. A sympathomimetic substance, enkephalin, that occurs in all parts of the human brain appears to be demonstrated.³⁴⁷

Neural control of the neurohypophysis¹¹⁷ and of the adenohypophysis¹¹⁸ is discussed, and it is demonstrated⁴¹ that the antidiuretic hormone in man can be released by emotional stress, hypertonic saline solution, acetylcholine and nicotine. While there are differences in reflex sympathetic responses to stimulation of the carotid sinus as opposed to direct hypothalamic stimulation, there is no proof that adrenal medullary secretion at rest differs materially from that due to carotid sinus stimulation.³³

By use of the technic of irrigation *in situ* the inhibitory effects of tetraethylammonium bromide within the adrenal gland are found to be localized in the terminal part of the adrenal secretory nervous system.¹⁹³ Both adrenal cortical and sex hormones have an excitant action on the pre- and post-ganglionic cervical sympathetic nerve fibers.⁸⁶

Integumentary System. Stimulation in the vicinity of the supraoptic hypothalamic nuclei of the sheep or the goat results in ejection of milk during lactation.^{8, 9} This effect is under hormonal control, as it remains unaltered in denervated udders. Commercial pitocin and pitressin or stimulation of the central vagi will also cause milk ejection.⁷

The chief factor in sweating is central stimulation of intact nerves, whereas peripheral influences such as temperature affect only limited areas.²⁶⁵ Sudomotor reflexes involving discharges from individual sweat pores show that emotional sweating may occur even during vasoconstriction, but heat regulatory sweating is always accompanied by vasodilatation.^{78, 79} Interruption of central excitatory reflex impulses results in defective regulation of sweating, heat production and blood pressure, but interruption of suprasegmental inhibitory impulses produces excessive reflex sweating and hypertension.²⁴⁶

Body responses to external heat utilize vasomotor adjustments until the surface temperature exceeds 34° C., when sweating supervenes.¹⁶ Heat of internal origin maintains the existing surface temperature and utilizes sweating proportionately. Sensations of heat, furthermore, do not parallel sweating caused by local heating. Afferent nerve fibers eliciting the sweating reflex, consequently, do not mediate heat sensation.¹⁴⁰

Following sympathectomy, local sweat responses to parasympathetic

drugs and to adrenin disappear, but exposure of the denervated skin to radiant heat will still induce definite local sweating.¹⁴⁶ After preganglionic sympathectomy, direct electrical stimulation of the foot pads in the cat causes sweating, and the response to pilocarpine is greater than normal.²⁷⁵ Six days after ganglionectomy and peripheral nerve section, however, the glands are not electrically excitable.

When regional evaporative rates from shaved skin areas are measured in nude subjects at a temperature of 27° C. low rates of movement of water of diffusion are exhibited uniformly on the arm, the leg and the trunk.²³⁸ High rates are shown on the palm, the sole and the face. The rates of water of diffusion correlate with the local blood supply. In a constant environment, sweating is usually limited to the distal parts of the lower extremities, but with increasing temperature it spreads up the legs and the trunk and finally to the arms and the face.²⁵⁰ During exposure to high environmental temperature evaporative heat losses are particularly great from the legs, the trunk and the forehead.⁸¹ Methods for local induction and quantitative analysis of human sweat are described,⁷¹ and the effects of intradermal injection of sympathomimetic agents on sweating are discussed.²⁸⁰ Temperature regulation of schizophrenic patients is more nearly normal after prefrontal lobotomy,³⁷ and sweating in gustatory areas is produced by histamine.²⁸⁷

Muscular System. In patients exhibiting autonomic dystonia, skeletal muscle fibrillation seems to be mediated by autonomic nerves.²⁰¹ Efforts to demonstrate a sympathetic innervation of the extrinsic ocular muscles yielded only negative results.³²

Sympathetic ganglionectomy is more effective and more lasting than preganglionic sympathectomy in modifying function of the smooth muscles of the cat's eye, and sensitization is never an important factor.¹⁶² The radial muscles of the iris in the cat following postganglionic sympathectomy are, however, slightly more sensitive to adrenin than after preganglionic sympathectomy.¹⁵⁸

Skeletal System. Stimulation of the lumbar sympathetic nerves in young dogs retards growth of the long bones of the leg, and unilateral lumbar sympathectomy results in increased length of these bones.¹¹¹ The effects are probably due to changes in the circulation.

CLINICAL

Clinical data reported during the past year indicate increasing recognition and understanding of autonomic dysfunction in the etiology and the courses of various diseases. Clinical syndromes associated with autonomic dysfunction have been outlined and discussed.^{43, 93, 200, 248, 266, 274, 284} The indications and the contraindications for surgical intervention and the limi-

tations of surgery involving autonomic nerves have also been more clearly outlined. The importance of careful selection of patients for treatment by autonomic neurosurgery has been emphasized. The physiologic effects of section of autonomic nerves are not fully known, but it is evident that limited sympathetic denervation may be carried out without serious functional damage.¹⁹⁹

Hypertension. Reports relative to sympathectomy in the treatment of hypertensive patients have been relatively few.^{29, 44, 88, 134, 135, 189, 204, 239, 314, 320, 323, 355} They consist chiefly of reviews of case histories and evaluations of this form of therapy based on follow-up studies. In general, the results obtained in properly selected patients have been gratifying, but general application of sympathectomy in hypertensive patients is shown to be inadvisable.

Peripheral Vascular Disease. Sympathectomy appears to have resulted in benefit to patients with arteriosclerosis,^{64, 82, 187} Raynaud's disease,^{20, 67, 271, 323} endarteritis obliterans,^{123, 236} articular rheumatism,³¹ frostbite³⁴⁹ and scleroderma.^{232, 233} The immediate results in many instances have been described as good. Follow-up studies, however, have revealed a relatively high percentage of late failures. Recurrence of vasoconstrictor activity in extremities following sympathectomy has been discussed.²⁵⁶ It can be explained most satisfactorily on the basis of sympathetic conduction pathways which do not traverse the sympathetic trunk.⁸³

Peptic Ulcer. Reports relative to vagotomy in the treatment of patients with gastric, duodenal and jejunal ulcers have been frequent.^{4, 18, 49, 53-56, 73, 119, 145, 148, 167, 169, 180, 197, 209, 234, 261, 277, 282, 283, 309-311} These reports indicate diversity of opinion regarding the value of this form of treatment. The most satisfactory results have been obtained by the use of vagotomy in conjunction with gastric resection or gastroenterostomy. Vagotomy is not to be regarded as a substitute for—but as an adjunct to—gastric resection or other surgical procedures^{119, 208}. It is not to be advised for patients with gastric ulcer, but is to be recommended particularly for patients with marginal ulcers.⁵⁴ Section of the posterior vagus nerve alone results in reduction in the hydrochloric acid content of the stomach comparable to that observed after section of both vagi.³⁰⁹ The necessity of section of the anterior vagus has, therefore, been questioned. The complications following vagotomy usually are trivial and self limited. Recurrence or persistence of duodenal ulcer after vagotomy is regarded as due to incomplete nerve section.⁷⁴ The future of vagotomy in the treatment of ulcer patients probably will be determined by whether or not there are serious persistent side effects.²⁷⁷ The clinical effects of splanchnicectomy in ulcer patients have also been discussed.^{240, 257}

Congenital Megacolon. The reported data support the assumption that

true congenital megacolon is associated with the absence of ganglia in the enteric plexuses in a zone near the distal end of the large intestine.^{10, 25, 152, 203, 225, 281, 286}

In view of the etiology of this disease, no benefit should be expected from sympathectomy. The most effective treatment involves resection of the portion of the large intestine which is devoid of enteric ganglia.

Bronchial Disease. The relative effectiveness of sympathectomy, vagotomy and resection of the pulmonary plexuses in patients with asthma has been considered.³²⁶ Bilateral resection of the vagus nerve⁴⁸ and bilateral resection of the posterior pulmonary plexus²²⁴ have yielded beneficial results in patients with intractable bronchial asthma. New data relative to the clinical physiology of the bronchi appear to support the assumption that pain of bronchial origin may be mediated through the vagi²¹¹ and that bronchospasm may persist after bilateral vagotomy.¹⁶⁵ These new data are somewhat at variance with current concepts. Massive collapse of the lungs following thoracic sympathectomy has been reported.¹⁹⁸

Sympathetic Nerve Blocking. Blocking of the sympathetic ganglia and nerves is employed extensively both as a diagnostic aid and as a therapeutic measure. Good results of blocking of the stellate ganglion have been reported in the treatment of patients with painful lesions of the upper extremity,²⁵³ pulmonary embolism,⁹⁰ occlusion of the central retinal artery,⁵¹ cerebro-vascular accidents^{223, 285} and cerebral concussion.²² Blocking of sympathetic trunk ganglia has also been employed in patients with neuralgia,²²³ multiple sclerosis,³³⁶ neuritis²⁴³ and early acute cholecystitis.⁷⁷ New data relative to the technic of sympathetic nerve blocking have been reported.^{2, 11, 170, 173, 214, 217, 278, 330, 341} Complications of stellate and thoracic sympathetic nerve blocks have also been described.^{19, 231, 325} In general, the immediate results of sympathetic nerve blocking are comparable to those of sympathectomy. The relief of pain due to vascular spasm is most striking in patients in whom the disease is of recent origin.¹¹⁶

Miscellaneous. An endoscopic surgical approach to the thoracic portion of the sympathetic trunk and the splanchnic nerves has been described.^{149, 176, 241} The technic of bilateral lumbar sympathectomy is also discussed.¹⁷⁴ The surgical significance of certain inhibitory respiratory reflexes that may arise during abdominal surgery²⁵³ and certain cardiosplanchnic reflexes²⁷ has been pointed out. Direct observation of sweating as a simple diagnostic test for peripheral nerve lesions is described.¹⁵⁴ Sweating after sympathectomy is explained on the basis of sympathetic pathways that are independent of the sympathetic trunk.³¹⁸ Cold applications are advised for the alleviation of pain due to hyperemia following sympathectomy.⁹⁵ Sympathectomized extremities are more susceptible to reductions in skin temperature during ether anesthesia than during spinal anesthesia. This is due to direct stimulation of the sympathetic ganglia or to the hypoxia of the

ganglia, blood vessels and sweat glands that are associated with general anesthesia. It may also be the result of the release of adrenin due to tissue asphyxia.⁹¹ The peripheral vasoconstriction caused by smoking is abolished in a sympathectomized limb.²⁵¹ The hypoxemic alterations in the electrocardiogram that are associated with certain brain injuries and other diseases appear to be related to hypoxemia of the myocardium rather than to a decrease in the flow of blood in the coronary arteries.²⁶⁷ New data have been advanced in support of the assumption that glaucoma is a manifestation of disturbed vasomotor function.²¹⁹ Chronic bulbous keratitis has been ameliorated by resection of the greater superficial petrosal nerve.¹⁵¹ Autonomic dysfunction in relation to otolaryngology³⁴⁰ and in relation to diseases of skeletal muscles³⁵² has been discussed. Disturbances in central autonomic centers, particularly in the diencephalon, have been found to be a factor in the pathogenesis of uremia.¹²⁶ Chronic sympathetic stimulation appears to facilitate the growth of melanoblastomas. It is suggested, therefore, that parasympathomimetic substances may be useful in the treatment of patients with malignant tumors.²⁶³ A hereditary factor in the etiology of sympathetic neuroblastoma appears to be indicated.³²⁴

Resection of the hypogastric plexus facilitates emptying of the urinary bladder.³⁰⁰ New data relative to its use for the relief of dysmenorrhea have been reported.²⁵⁹ The technic of hypogastric resection has also been discussed.³¹³ Favorable results have been reported of vagotomy in patients with idiopathic ulcerative colitis^{80, 296} and patients with recurrent acute pancreatitis.²⁰⁵ Interruption of a pernicious cycle of pain appears to be a major factor in the relief of anginal symptoms by sympathectomy.⁸⁹ Resection of the aortic plexus for the relief of angina pectoris has been reported.⁶⁸ The heart rate and respiration may be disturbed reflexly in children by mechanical irritation of the nasopharynx, the trachea, the bronchi or the esophagus.²⁶⁴ The diagnostic and the therapeutic value of viscerocutaneous and cutaneo-visceral reflexes is pointed out.^{332, 353}

Stress situations frequently cause exercise intolerance and cardiac hyperactivity that may be relieved by the achievement of relaxation and a feeling of security.⁷⁶ In emotionally tense subjects the exudation rate of liquids in the skin is increased. Relaxing suggestions or distractive conversation result in a decrease in the exudation rate.¹⁵⁹ In mentally ill patients, changes in the clinical psychologic status are accompanied by parallel changes in autonomic functions.⁹⁸

REFERENCES

- ¹ Adams-Ray, J. and Norlen, G.: Bladder distention reflex with vasoconstriction in cutaneous venous capillaries. *Acta physiol. Scandinav.* 23:95-109, 1951.
- ² —, and Hjelmstrom, P.: Mécanisme de l'action du blocage du sympathique sur l'oedème traumatique. *Presse méd.* 56:1206-1208, 1951.

- ³ Alexander, W. F. and Backlar, B.: Nucleic acid changes in rat nerve tissue after parenteral administration of vitamin B₁₂. *Proc. Soc. Exper. Biol. & Med.* 78:181-184, 1951.
- ⁴ Allen, A. W.: Present concepts concerning the surgical management of duodenal ulcer. *New England J. Med.* 245:591-594, 1951.
- ⁵ Ambache, N.: Unmasking, after cholinergic paralysis by Botulinum toxin, of a reversed action of nicotine on the mammalian intestine, revealing the probable presence of local inhibitory ganglion cells. *Brit. J. Pharmacol.* 6:51-67, 1951.
- ⁶ Anand, B. K. and Brobeck, J. R.: Localization of a feeding center in the hypothalamus of the rat. *Proc. Soc. Exper. Biol. & Med.* 77:323-324, 1951.
- ⁷ Andersson, B.: Some observations on the neuro-hormonal regulation of milk ejection. *Acta physiol. Scandinav.* 23:1-7, 1951.
- ⁸ —: The effect and localization of electrical stimulation of certain parts of the brain stem in sheep and goats. *Acta physiol. Scandinav.* 23:8-23, 1951.
- ⁹ —: Further studies on the milk ejection mechanism in sheep and goats. *Acta physiol. Scandinav.* 23:24-30, 1951.
- ¹⁰ Andreassen, M. and Kromann, B.: Hirschsprung's disease, Congenital of Colon. Review. *Ugesk. f. læger.* 112:1553-1557, 1950.
- ¹¹ Ansbro, F. P. and Mendoza, G. T.: Continuous paravertebral lumbar sympathetic block. Report of six cases. *J. Missouri M. A.* 47:889-891, 1950.
- ¹² Atanacković, D. and Dalgaard-Mikkelsen, S.: Chemoreceptors and acetylcholine hypertension. *Acta physiol. Scandinav.* 22:77-78, 1951.
- ¹³ Auer, J.: Postnatal cell differentiation in the hypothalamus of the hamster. *J. Comp. Neurol.* 95:17-42, 1951.
- ¹⁴ Bayer, R. and Hoff, F.: Die vegetativ-neurale Steuerung der menschlichen Gebärmutter. *Wien. klin. Wchnschr.* 63:275-278, 1951.
- ¹⁵ Bazett, H. C.: Theory of reflex controls to explain regulation of body temperature at rest and during exercise. *J. Physiol.* 4:245-262, 1951.
- ¹⁶ —: A theory of reflex control of temperature at rest and during exercise. *Federation Proc.* 10:152, 1951.
- ¹⁷ Bernthol, T. and Woodcock, C. C., Jr.: Responses of the vasomotor center to hypoxia after denervation of carotid and aortic bodies. *Am. J. Physiol.* 166:45-54, 1951.
- ¹⁸ Bingham, J. R., Ingelfinger, F. J., and Smithwick, R. H.: Effect of combined sympathectomy and vagectomy on the gastro-intestinal tract. *J.A.M.A.* 146:1406-1408, 1951.
- ¹⁹ Bischof, W.: Komplikationen nach Stellatumblockaden. *Acta neuroveg.* 2:357-365, 1951.
- ²⁰ Blain, A., Coller, F. A., and Carver, G. B.: Raynaud's disease. A study of criteria for prognosis. *Surgery.* 29:387-397, 1951.
- ²¹ Block, M. A., Wakim, K. G., and Mann, F. C.: Effect of stimulation of renal nerves on renal circulation and function. *Federation Proc.* 10:16, 1951.
- ²² Blumensaat, C.: Zur Behandlung der Folgen der Commotio cerebri mit der Halsgrenzstrangblockade. *Zentralbl. f. Chir.* 76:498-504, 1951.
- ²³ — und Menzel, E.: Rückenmarkverletzung und motorische Innervation der oberen Harnwege. *Längenbeck's Arch. u. deutsche. Ztschr. f. Chir.* 269:87-121, 1951.
- ²⁴ Bodian, D.: Nerve endings, neurosecretory substance and lobular organization of the neurohypophysis. *Bull. Johns Hopkins Hosp.* 89:354-376, 1951.
- ²⁵ Bodian, M.: Hirschsprung's disease. *Gastroenterologia.* 76:339-343, 1951.

- ²⁶ —, Carter, C. O., and Ward, B. C. H.: Hirschsprung's disease. *Lancet*. 260:302-309, 1951.
- ²⁷ Boeke, J.: Sympathetic Grundplexus contra Terminalreticulum. *Acta neuroveg.* 2:32-40, 1951.
- ²⁸ Borison, H. L. and Brizzee, K. R.: Morphology of emetic chemoreceptor trigger zone in cat medulla oblongata. *Proc. Soc. Exp. Biol. & Med.* 77:38-42, 1951.
- ²⁹ Boyd, A. M.: The surgery of hypertension. *Practitioner*. 166:564-570, 1951.
- ³⁰ Bozler, E. and Burch, B. H.: Role of the vagus in the control of respiration. *Am. J. Physiol.* 166:255-261, 1951.
- ³¹ Braeucker, W.: Der Gelenkrheumatismus als vegetative Regulationsstörung. *Med. Klin.* 46:41-44, 1951.
- ³² Brehm, A. und Büchsel, H.: Untersuchungen über die Wirkung von Kurzwellen-durchblutungen peripherer und zentraler Anteile des vegetativen Nervensystems. *Acta neuroveg.* 2:366-376, 1951.
- ³³ Brücke, F.: Über Unterschiede zwischen zentraler und reflektorischer Sympathikus-erregung. *Deutsche med. Wchnschr.* 75:1547-1549, 1950.
- ³⁴ Brown, G. L.: The sympathetic innervation of the extrinsic ocular muscles. *J. Physiol.* 112:211-214, 1951.
- ³⁵ Bruce, H. M. and Kennedy, G. C.: The central nervous control of food and water intake. *Proc. Roy. Soc., London, s.B.*, 138:528-544, 1951.
- ³⁶ Brunaud, M. et Dussardier, M.: Recherches sur le médiateur chimique du nerf pneumogastrique des ruminants. *J. de physiol.* 43:281-302, 1951.
- ³⁷ Buck, C. W., Carscallen, H. B., and Hobbs, G. E.: Effect of prefrontal lobotomy on temperature regulation in schizophrenic patients. *Arch. Neurol. & Psychiat.* 65:197-205, 1951.
- ³⁸ Carpenter, F. G.: Histological changes in parasympathetically denervated feline bladder. *Am. J. Physiol.* 166:692-698, 1951.
- ³⁹ — and Root, W. S.: Effect of parasympathetic denervation on feline bladder function. *Am. J. Physiol.* 166:686-691, 1951.
- ⁴⁰ Celander, O. and Folkow, B.: Are parasympathetic vasodilator fibers involved in depressor reflexes elicited from the baroreceptor regions? *Acta physiol. Scandinav.* 23:64-77, 1951.
- ⁴¹ Chalmers, T. M. and Lewis, A. A. G.: Stimulation of the supraoptico-hypophyseal system in man. *Clin. Sc.* 10:127-135, 1951.
- ⁴² Chauchard, B. et Chauchard, P.: Action des hormones sexuelles et corticosurrénales sur les fibres nerveuses sympathiques. *Compt. rend. Soc. de biol.* 145:655-656, 1951.
- ⁴³ Chorobski, J.: The syndrome of crocodile tears. *Arch. Neurol. & Psychiat.* 65:299-318, 1951.
- ⁴⁴ Chris, S. M.: Sympathetomy for hypertension. *Brit. M. J.* 1:665-670, 1951.
- ⁴⁵ Christensen, K. and Lewis, E.: Intracranial vascular nerves from cranial nerve roots. *Anat. Rec.* 109:19, 1951.
- ⁴⁶ —, and Kuntz, A.: Innervation of the renal blood vessels in the cat. *J. Comp. Neurol.* 95:373-375, 1951.
- ⁴⁷ Cicardo, V. H.: Localisation des centres spinaux vasoconstricteurs par excitation chimique. *Compt. rend. Soc. de biol.* 145:588-589, 1951.
- ⁴⁸ Clarke, C. A.: Bronchial asthma treated by bilateral resection of the vagus. A report of six cases. *Lancet*, 260:438-440, 1951.
- ⁴⁹ Colp, R.: Surgical management of duodenal ulcer. *Rev. Gastroenterol.* 18:724-732, 1951.

- ⁵⁰ Corona, G. L.: Contributo alla conoscenza della struttura e della innervazione della neuroipofisi. *Ztschr. f. Anat. u. Entwicklungsgesch.* 115:658-675, 1951.
- ⁵¹ Coston, T. O.: Ocular symptoms of stellate ganglion block. Its use in the treatment of occlusion of the central retinal artery. *Am. J. Ophth.* 34:1289-1293, 1951.
- ⁵² Coujard, R.: Recherches sur les plexus nerveux de l'intestin. *Arch. Anat. microscopique et Morphol. Expér.* 39:110-151, 1951.
- ⁵³ Crile, G., Jr.: Technique of vagotomy and gastroenterostomy in the treatment of duodenal ulcer. *Surg., Gynec. & Obst.* 92:309-313, 1951.
- ⁵⁴ — and Brown, G. M., Jr.: Vagotomy as a treatment for marginal ulcer. *Gastroenterology*. 17:14-19, 1951.
- ⁵⁵ — and Miller, D. W.: Vagotomy in the treatment of biliary dyskinesia. *Arch. Surg.* 63:687-694, 1951.
- ⁵⁶ Dailey, U. G.: Phrenic nerve crush as adjunct to vagotomy in treatment of peptic ulcer. *J. Internat. Coll. Surgeons*. 14:600-602, 1950.
- ⁵⁷ Daly, M. de B. and Mount, L. E.: The origin, course and nature of bronchomotor fibers in the cervical sympathetic nerve of the cat. *J. Physiol.* 113:43-62, 1951.
- ⁵⁸ — and Schweitzer, A.: Effects of sino-aortic nerve stimulation on the bronchi. *Acta physiol. Scandinav.* 22:66-72, 1951.
- ⁵⁹ —: Reflex bronchomotor responses to stimulation of receptors in the regions of the carotid sinus and arch of the aorta in the dog and cat. *J. Physiol.* 113:442-462, 1951.
- ⁶⁰ Daniel, P. M. and Prichard, M. M. L.: Effects of stimulation of the hepatic nerves and of adrenaline upon the circulation of the portal venous blood within the liver. *J. Physiol.* 114:538-548, 1951.
- ⁶¹ Danon, D.: Variations de la structure des synapses dans les ganglions sympathiques chez l'homme. *Acta anat.* 13:163-170, 1951.
- ⁶² Dawson, H. and Matchett, P. A.: The control of the intraocular pressure in the rabbit. *J. Physiol.* 113:387-397, 1951.
- ⁶³ Deaton, W. R., Jr., Postlethwait, R. W., and Bradshaw, H. H.: Gastric secretion and motility in dogs post-vagotomy—two year study. *Gastroenterology*. 17:72-76, 1951.
- ⁶⁴ De Bakey, M. E., Creech, O., and Woodhall, J. P.: Sympathectomy in arteriosclerotic peripheral vascular disease. *J.A.M.A.* 144:1227-1231, 1950.
- ⁶⁵ De Castro, F.: Sur la structure de la synapse dans les chemorecepteurs: leur mécanisme d'excitation et rôle dans la circulation sanguine locale. *Acta physiol. Scandinav.* 22:14-43, 1951.
- ⁶⁶ De Groot, J. and Harris, G. W.: Hypothalamic control of anterior pituitary gland and blood lymphocytes. *J. Physiol.* 111:335-375, 1950.
- ⁶⁷ De la Fuente Chaos, A. y Garcia Diaz, S.: Estudio crítico de la gangliectomía en los procesos isquémicos de los miembros. *Bol. Cultural e Informativo, Consejo General de Colegios Médicos de España*. 11:51-57, 1951.
- ⁶⁸ Demmer, F.: Die transsternale Sympathektomie und Sympathikodiaphtherese an der Aorta bei Angina pectoris. *Wien. klin. Wchnschr.* 63:719-723, 1951.
- ⁶⁹ De Vanna, F.: Distribuzione periferica del nervo terminale e sue cellule nei mammiferi. *Arch. ital. anat. e embriol.* 56:1-20, 1951.
- ⁷⁰ Dirken, M. N. J. and Woldring, S.: Unit activity in bulbar respiratory centre. *J. Neurophysiol.* 14:211-225, 1951.
- ⁷¹ Dole, V. P., Stall, B. G., and Schwartz, I. L.: Methods for local induction and quantitative analysis of human sweat. *Proc. Soc. Exper. Biol. & Med.* 77:412-415, 1951.
- ⁷² Dornhorst, A. C. and Sharpey-Schafer, E. P.: Collateral resistance in limbs with

arterial obstruction: Spontaneous changes and effects of sympathectomy. *Clin. Sc.* 10:371-381, 1951.

- ⁷³ Dorton, H. E. and Webb, J. G.: Vagotomy and pyloroplasty: Physiologic treatment for duodenal ulcer. *Kentucky M. J.* 49:139-147, 1951.
- ⁷⁴ Dragstedt, L. R. and Woodward, E. R.: Appraisal of vagotomy for peptic ulcer after seven years. *J.A.M.A.* 145:795-802, 1951.
- ⁷⁵ Driver, R. L. and Vogt, M.: Carotid sinus reflex and contraction of the spleen. *Brit. J. Pharmacol.* 5:505-509, 1951.
- ⁷⁶ Duncan, C. H., Stevenson, I. P., and Wolff, H. G.: Life situations, emotions, and exercise tolerance. *Psychosom. Med.* 8:36-50, 1951.
- ⁷⁷ Eastwood, D. and Womak, N. A.: Sympathetic nerve block in early acute cholecystitis. *Arch. Surg.* 63:128-138, 1951.
- ⁷⁸ Ebbecke, U.: Sudomotorische Reflexe. *Proc. 18th Internat. Physiol. Cong.* p. 539, 1950.
- ⁷⁹ —: Arbeitsweise der Schweißdrüsen und sudomotorische Reflexe bei unmittelbarer Beobachtung mit Lupenvergrößerung. *Arch. f. d. ges. Physiol.* 253:333-350, 1951.
- ⁸⁰ Eddy, F. D.: Late results of vagotomy in the treatment of idiopathic ulcerative colitis and regional enteritis. *Surgery.* 29:11-23, 1951.
- ⁸¹ Ederstrom, H. E., Hertzman, A. B., and Randall, W. C.: Further studies in the regional distribution of heat losses. *Am. J. Physiol.* 163:709-710, 1950.
- ⁸² Edwards, E. A. and Crane, C.: Lumbar sympathectomy for arteriosclerosis of the lower extremities. *New England J. Med.* 244:199-204, 1951.
- ⁸³ Ehrlich, E., Jr. and Alexander, W. F.: Surgical implications of upper thoracic independent sympathetic pathways. *Arch. Surg.* 62: 609-614, 1951.
- ⁸⁴ Eichner, D.: Zur Frage der Neurosekretion der Ganglienzellen des Nebennierenmarkes. *Ztschr. f. Zellforsch.* 36:293-297, 1951.
- ⁸⁵ Eliasson, S., Folkow, B., Lindgren, P., and Uvnäs, B.: Activation of sympathetic vasodilator nerves to skeletal muscles in the cat by hypothalamic stimulation. *Acta physiol. Scandinav.* 23:333-351, 1951.
- ⁸⁶ Engelbrecht, W.: Über Zahl und Deutung degenerierter Ganglienzellen in sympathektomierten Grenzstrangganglien. *Klin. Wchnschr.* 29:41-49, 1951.
- ⁸⁷ Eränkő, O.: Histochemical evidence of intense phosphatase activity in the hypothalamic magno-cellular nuclei of the rat. *Acta physiol. Scandinav.* 24:1-6, 1951.
- ⁸⁸ Evans, J. A.: The place of splanchnicectomy in the treatment of hypertension. *Canad.M.A.J.* 64:47-50, 1951.
- ⁸⁹ —, Poppen, J. L., and Tobias, J. B.: Relief of angina pectoris by sympathectomy. *J.A.M.A.* 144:1432-1436, 1950.
- ⁹⁰ Faxon, H. H., Flynn, J. H., and Anderson, R.: Stellate block as an adjunct to the treatment of pulmonary embolism. *New England J. Med.* 244:586-590, 1951.
- ⁹¹ Felder, D. A., Linton, R. R., Todd, D. P., and Banks, C.: Changes in the sympathectomized extremity with anesthesia. *Surgery.* 29:803-810, 1951.
- ⁹² Field, E. J.: The nervous component of the atrioventricular bundle. *J. Anat.* 85:105-112, 1951.
- ⁹³ Fischer-Brügge, E. und Sunder-Plassman, P.: Die zentrale vasomotorische Beeinflussung umschriebener peripherer Körperabschnitte und ihre klinische Bedeutung. *Acta neuroveg.* 1:374-388, 1950.
- ⁹⁴ Flerko, B.: Einfluss experimenteller Hypothalamuslaesionen auf das Eileiterepithel. *Acta morphol.* 1:5-14, 1951.
- ⁹⁵ Fontaine, R., Dany, A., Muller, J. N., et Kieny, R.: De l'influence de réactions

- vaso-motrices périphériques sur les phénomènes douloureux dans un cas d'algies diffusantes. *Rev. chir.* 70:328-336, 1951.
- ⁹⁶ Frenckner, P.: Observations on anatomy of the tympanic plexus and technique of tympanosympathectomy. *Arch. Otolaryng.* 54:347-355, 1951.
 - ⁹⁷ Frowein, R. and Klar, E.: Ueber vegetative Erscheinungen bei der praefrontalen Leukotomie. *Klin. Wchnschr.* 29:245-249, 1951.
 - ⁹⁸ Funkenstein, D. H., Greenblatt, M., and Solomon, H. C.: Autonomic changes paralleling psychologic changes in mentally ill patients. *J. Nerv. & Ment. Dis.* 114:1-18, 1951.
 - ⁹⁹ Gatenby, J. B. and Moussa, T. A. A.: The sympathetic ganglion cell, with Sudan black and the Zernike microscope. *J. Roy. Micr. Soc.* 70:342-364, 1951.
 - ¹⁰⁰ —: The neurone of the human autonomic system and the so-called "senility pigment." *J. Physiol.* 114:252-254, 1951.
 - ¹⁰¹ Gellert, A.: Quelques observations sur le ganglion caverneux à la suite de nouvelles recherches. *Acta morphol.* 1:15-22, 1951.
 - ¹⁰² Gohegan, W. A. and Aidar, O.: Splanchnic afferent pathways in the central nervous system. *Anat. Rec.* 109:35-36, 1951.
 - ¹⁰³ Girling, F.: Sympathetic stimulation and critical closing pressure. *Federation Proc.* 10:50, 1951.
 - ¹⁰⁴ Glass, G. B. J., Mersheimer, W. L., and Svigals, C. S.: Effect of vagotomy and subtotal gastric resection on the secretion of mucin in the human stomach. *Arch. Surg.* 62:658-669, 1951.
 - ¹⁰⁵ Goetz, K.: Ein anatomischer Beitrag zur Innervation des M. sphincter ani internus. *Zentralbl. f. Chir.* 76:802-807, 1951.
 - ¹⁰⁶ Goetzl, F. R. and Bien, C.: Changes in blood pressure in response to presumably and to potentially painful stimuli. *Federation Proc.* 10:51, 1951.
 - ¹⁰⁷ — and Lu, G.: Changes in blood pressure in response to presumably painful stimuli. *J. Physiol.* 4:161-170, 1951.
 - ¹⁰⁸ Green, J. D.: The comparative anatomy of the hypophysis, with special reference to its blood supply and innervation. *Am. J. Anat.* 88:225-290, 1951.
 - ¹⁰⁹ Greer, M. A.: Evidence of hypothalamic control of the pituitary release of thyrotropin. *Proc. Soc. Exper. Biol. & Med.* 77:603-608, 1951.
 - ¹¹⁰ Greving, R.: Histologische Studien am Plexus myentericus des Magens. 2. Das Problem de Ganglienzellfortsätze. *Ztschr. f. Anat. u. Entwicklungsgesch.* 115:541-554, 1951.
 - ¹¹¹ Gullickson, G., Kubicek, W. G., and Kottke, F. J.: Effects of stimulation of lumbar sympathetic nerves on longitudinal bone growth in dogs. *Federation Proc.* 10:56, 1951.
 - ¹¹² Gunn, M.: A study of the enteric plexuses in some amphibians. *Quart. J. Micr. Sc.* 92:55-77, 1951.
 - ¹¹³ Guyton, A. C., Batson, H. M., and Smith, C. M.: Adjustments of the circulatory system following very rapid transfusion or hemorrhage. *Am. J. Physiol.* 164:351-359, 1951.
 - ¹¹⁴ — and Armstrong, G. G.: Method for studying competence of the body's blood pressure mechanisms and effect of pressoreceptor denervation. *Am. J. Physiol.* 164:360-368, 1951.
 - ¹¹⁵ — and Harris, J. W.: Pressoreceptor-autonomic oscillation: a probable cause of vasomotor waves. *Am. J. Physiol.* 165:158-166, 1951.
 - ¹¹⁶ Harned, B. W. and Theis, F. V.: A study of sympathetic blocks. *J. Missouri M. A.* 48:882-886, 1951.

- ¹¹⁷ Harris, G. W.: Neural control of the pituitary gland: I. The neurohypophysis. *Brit. M. J.* 2:559-564, 1951.
- ¹¹⁸ —: Neural control of the pituitary gland: II. The adenohypophysis, with special reference to the secretion of ACTH. *Brit. M. J.* 2:627-634, 1951.
- ¹¹⁹ Harth, H.: Beitrag zur Vagotomiefrage. *Wien. klin. Wchnschr.* 63:508-509, 1951.
- ¹²⁰ Harting, K.: Zur Frage der Zweikernigkeit sympathischer Ganglienzellen. III. *Ztschr. f. Zellforsch.* 36:268-272, 1951.
- ¹²¹ Heifetz, M. D.: Autonomic phenomenon noted during cerebral angiography. *Bull. Los Angeles Neurol. Soc.* 16:251-252, 1951.
- ¹²² Helbig, D.: Reizung vegetativer Zentren bei Ultraschallbehandlung des Gehirns debiler Kinder. *Arch. f. Kinderheilk.* 142:145-153, 1951.
- ¹²³ Herget, R.: Früh- und Spätergebnisse nach Grenzstrangresektion bei Endangitis obliterans und Arteriosklerose. *Langenbeck's Arch. u. Deutsch. Ztschr. f. Chir.* 268:394-408, 1951.
- ¹²⁴ Hermann, H.: Mikroskopische Studien am Grenzstrang des Sympathikus beim Menschen. *Anat. Anz.* 98:181-185, 1951.
- ¹²⁵ —, Vial, J. et Chatonnet, J.: Influence du travail musculaire sur l'action intestino-inhibitrice de l'adrénaline. *Compt. rend. Soc. de biol.* 144:1062-1063, 1950.
- ¹²⁶ Hess, L.: The relationship of the vegetative nervous system to uremia. *J. Nerv. & Ment. Dis.* 113:136-143, 1951.
- ¹²⁷ Hess, W. R.: Principien organischer ordnung am Beispiel des vegetativen Nervensystems. *Klin. Wchnschr.* 29:105-111, 1951.
- ¹²⁸ Heymans, C.: Chemoreceptors and regulation of respiration. *Acta physiol. Scandinav.* 22:4-13, 1951.
- ¹²⁹ Hill, R. T.: The route of the nerves to the ovary in small animals. *Anat. Rec.* 109:44, 1951.
- ¹³⁰ Hoenig, W.: Über den reflektorischen Wirkungsmechanismus des ultraschalls am vegetativen Nervensystem. *München. med. Wchnschr.* 93:1743-1746, 1951.
- ¹³¹ Hoff, E. C., Kell, J. F., Jr., Hastings, N., Sholes, D. M., and Gray, E. H.: Vasomotor, cellular and functional changes produced in kidney by brain stimulation. *J. Neurophysiol.* 14:317-332, 1951.
- ¹³² Hoff, H.: Die Bedeutung der zentral-vegetativen Steuerung beim Menschen. *Wien. klin. Wchnschr.* 63:175-180, 1951.
- ¹³³ Honjin, R.: Studies on the nerve endings in the small intestine. *Cytological and Neurological Studies. U. of Kanazawa, No. 9:*1-14, 1951.
- ¹³⁴ Hoobler, S. W., Manning, J. T., Paine, W. G., Helcher, P. O., McClellan, S. G., Renfert, H., Jr., Kahn, E. A., and Peet, M. M.: Observations on sixty patients with hypertension successfully treated by splanchnicectomy. *Univ. Michigan M. Bull.* 16:381-386, 1950.
- ¹³⁵ —, McClellan, S. G., Helcher, P. O., Renfert, H., Peet, M. M., and Kahn, E. A.: The effects of splanchnicectomy on the blood pressure in hypertension. *Circulation.* 4:173-183, 1951.
- ¹³⁶ Houck, C. R.: Lack of evidence of a Trueta shunt in dogs during stimulation of renal artery nerves. *Federation Proc.* 10:66-67, 1951.
- ¹³⁷ Hukuhara, T., Nakayama, S., Baba, S., and Odanaka, T.: On the localization of the respiratory center. *Japanese J. Physiol.* 2:44-49, 1951.
- ¹³⁸ Ingersoll, E. H., Hegre, E. S., and Jones, L.: Bladder activity of the cat in response to forebrain stimulation. *Anat. Rec.* 109:47-48, 1951.

- ¹³⁹ Irwin, J. H.: Conservative sympathectomy as an antiallergic measure. *Med. Rec.* 163:297-305, 1950.
- ¹⁴⁰ Issekutz, B., Hetényi, G., and Diosy, A.: The physiology of sweat secretion. *Arch. internat. de pharmacodyn.* 83:133-134, 1950.
- ¹⁴¹ Jabonero, V.: La doble constitucion (neuronal y sincicial) del sistema neurovegetativo periferico. Extraído do Arquivo de Anatomia e Antropologia. 27:75-105, 1950.
- ¹⁴² —: Étude sur la morphopathologie des cellules interstitielles du système neurovégétatif périphérique. I. *Biologica Latina.* 4:323-356, 1951.
- ¹⁴³ —: Études sur le système neurovégétatif périphérique. III. Innervation de l'estomac humain. *Acta anat.* 11:490-532, 1951.
- ¹⁴⁴ —: Études sur le système neurovégétatif périphérique. IV. Innervation intermurale de la vesicule biliaire humaine. *Acta anat.* 13:171-192, 1951.
- ¹⁴⁵ Jahn, D.: Die konstitutionelle Grundlage des Ulcus ventriculi und duodeni. *Med. Klin.* 46:65-70, 1951.
- ¹⁴⁶ Janowitz, H. D. and Grossman, M. I.: An exception to Cannon's law. *Experientia.* 7:275, 1951.
- ¹⁴⁷ — and Hollander, F.: Critical evidence that vagal stimulation does not release gastrin. *Proc. Soc. Exper. Biol. & Med.* 76:49-52, 1951.
- ¹⁴⁸ Jefferson, N. C., Phillips, C. W., Proffett, M. M., and Necheles, H.: The effects of vagotomy and phrenicotomy on the cardia. *Am. J. Digest. Dis.* 18:217-219, 1951.
- ¹⁴⁹ Job, C. and Villniger, R.: Die endoskopisch-transpleurale Sympathikotomie nach E. Kux beim Ulcus duodeni und ihre therapeutischen Ergebnisse. *Deutsch. med. Wchnschr.* 76:734-736, 1951.
- ¹⁵⁰ John, E.: Schädel-Hirutrauma, vegetatives Nervensystem und Ausnahmezustände. *Acta neuroveg.* 2:163-170, 1951.
- ¹⁵¹ Johnson, L. V. and Nosik, W. A.: Greater superficial petrosal neurectomy for relief of chronic bulbous keratitis. *Arch. Opth.* 45:32-39, 1951.
- ¹⁵² Johnston, J. H., Jr.: Hirschsprung's disease. *Mississippi Doctor.* 29:103-107, 1951.
- ¹⁵³ Jourdan, F. et Collet, A.: Evolution de la pression arterielle chez le chien apres la suppression de ses mecanismes nerveux regulateurs. *J. de physiol.* 43:149-298, 1951.
- ¹⁵⁴ Kahn, E. A.: Direct observation of sweating in peripheral nerve lesions; its use as a simple diagnostic test. *Surg., Gynec. & Obst.* 92:22-26, 1951.
- ¹⁵⁵ Kaada, B. R.: Somatomotor, autonomic and electrocorticographic responses to electrical stimulation of rhinencephalic and other structures in primates, cat and dog. *Acta physiol. Scandinav.* 23, Suppl., 83:1-285, 1951.
- ¹⁵⁶ Kaplan, S. A., Fomon, S. J., and Rapaport, S.: Effect of splanchnic nerve division on urinary excretion of electrolytes during mannitol loading in the hydropenic dog. *Am. J. Physiol.* 166:641-648, 1951.
- ¹⁵⁷ Kehler, E.: Schützt die paravertebrale Sympathektomie im obersten Seitenhorngebiet vor postoperativen Reflexatelektasen. *Zentralbl. f. Chir.* 76:648-660, 1951.
- ¹⁵⁸ Kennedy, G. C.: The hypothalamic control of food intake in rats. *Proc. Roy. Soc. Med.* 137:535-549, 1950.
- ¹⁵⁹ Kepecs, J. G., Robin, M., and Brunner, M. J.: Relationship between certain emotional states and exudation into the skin. *Psychosom. Med.* 8:10-17, 1951.
- ¹⁶⁰ Kimmel, D. L. and Moyer, E. K.: The course of visceral branches of sacral nerves to the urinary bladder in human fetuses. *Anat. Rec.* 109:50, 1951.

- ¹⁶¹ Kirgis, H. D.: The reaction of sympathectomized smooth muscle to graded doses of adrenalin. *Anat. Rec.* 109:50-51, 1951.
- ¹⁶² —, Reed, A. F., and Pearce, J. Y.: The relative effectiveness of sympathetic ganglionectomy and section of preganglionic fibers in inactivation of smooth muscle. *Surgery.* 28:941-949, 1950.
- ¹⁶³ Kiss, T.: Experimentell-Morphologische Analyse der Nebenniereninnervation. *Acta anat.* 13:81-89, 1951.
- ¹⁶⁴ Kladetzky, J.: Über die Innervation des Ovariums. *Arch. f. Gynäkol.* 179:363-384, 1951.
- ¹⁶⁵ Klassen, K. P., Morton, D. R., and Curtis, G. M.: The clinical physiology of the human bronchi. III. The effect of vagus section on the cough reflex, bronchial caliber, and clearance of bronchial secretions. *Surgery.* 29:483-490, 1951.
- ¹⁶⁶ Klinge, F. M.: Defecation in animals following excision of Auerbach's plexus in the colon. *Federation Proc.* 10:74, 1951.
- ¹⁶⁷ Klingenstein, P., Colp, R., Druckerman, J., and Weinstein, V. A.: Observations on gastrectomy for chronic duodenal ulcer with particular reference to gastrectomy with and without infradiaphragmatic vagotomy. *J. Mt. Sinai Hosp.* 17:429-441, 1951.
- ¹⁶⁸ Kloppe, P. J.: Pupil dilation caused by stimulation of sensory nerves in frogs. *Acta physiol. et pharmacol. neerl.* 2:13-18, 1951.
- ¹⁶⁹ Knox, G. and West, J. P.: Vagus section in the treatment of gastrojejunal ulcer. *Ann. Surg.* 133:216-218, 1951.
- ¹⁷⁰ Köhler, G.: Ein Beitrag zur Anaesthesie am sympathischen Nervensystem. *Therap. der Gegenwart.* 7:262-264, 1951.
- ¹⁷¹ Konzett, H.: Sympathicomimetica und Sympathicolytica am isoliert durchströmten Ganglion cervicale superius der Katze. *Helvet. physiol. et pharmacol. acta.* 8:245, 1950.
- ¹⁷² Koppen, K.: Die Nerven im normalen und transplantierten Ovar des Kaninchens. *Arch. f. Gynäkologie.* 179:478-486, 1951.
- ¹⁷³ Kuntz, E. H.: Kontralateraler Pneumothorax nach Stellatumblockade. *Zentralbl. Chir.* 76:1015-1018, 1951.
- ¹⁷⁴ Kunlin, J. et Froehlich, F.: La sympathectomie lombaire bilatérale par voie médiane extra-péritonéale (d'après 102 cas). *J. Chir.* 67:696-701, 1951.
- ¹⁷⁵ Kuntz, A.: Afferent innervation of peripheral blood vessels through sympathetic trunks. *South. M. J.* 44:673-678, 1951.
- ¹⁷⁶ Kux, E.: The endoscopic approach to the vegetative nervous system and its therapeutic possibilities, especially in duodenal ulcer, angina pectoris, hypertension and diabetes. *Dis. of Chest.* 20:139-147, 1951.
- ¹⁷⁷ Kwerch H. und Leibetseder, F.: Vegetatives Nervensystem und Blutsteuerung. *Wien. klin. Wchnschr.* 63:309-310, 1951.
- ¹⁷⁸ Landau, E.: Contribution a l'innervation du coeur (fibres myélinisées). *Acta anat.* 13:119-124, 1951.
- ¹⁷⁹ Langley, L. L. and Whiteside, J. A.: Mechanism of accommodation and tone of urinary bladder. *J. Neurophysiol.* 14:147, 1951.
- ¹⁸⁰ Larsen, R. M.: Surgical treatment of peptic ulcer. *South. M. J.* 44:1016-1021, 1951.
- ¹⁸¹ Lim, R. K. S. and Mozer, P.: Does vagus excitation liberate pyloric gastrin? *Federation Proc.* 10:84, 1951.
- ¹⁸² Linde, S.: Studies on the stimulation mechanism of gastric secretion. *Acta physiol. Scandinav.* 21:Suppl. 74.

- 183 Lipp, W.: Studien zur Herzinnervation. I. Die Innervation der Pulmonalisklappen. *Acta anat.* 13:30-62, 1951.
- 184 Loffredo-Sampaolo, C.: Studio istologico sulla fine innervazione sensitiva delle tuniche esofagee. *Boll. Soc. ital. biol. sper.* 27:479-482, 1951.
- 185 Lowenberg, R. I. and Morton, D. E.: The anatomic and surgical significance of the lumbar sympathetic nervous system. *Ann. Surg.* 133:525-532, 1951.
- 186 Lowenstein, O. and Loewenfeld, I. E.: Types of central autonomic innervation and fatigue. Pupillographic studies. *Arch. Neurol. & Psychiat.* 66:580-599, 1951.
- 187 MacCarty, C. S., Janes, J. M., and Allen, E. V.: Treatment of arteriosclerotic popliteal aneurysm by lumbar sympathectomy and extirpation at the same operative session. *Postgrad. Med.* 10:25-30, 1951.
- 188 Magnenat, P.: Étude neurohistologique du poulmon. *Acta anat.* 13:193-224, 1951.
- 189 Mallet-Guy, P. et Durand, L.: Documents pour la justification de la splanchnicectomie droite dans les états d'hypotonie des voies biliaires. *Lyon chir.* 46:791-804, 1951.
- 190 Malmejac, J. et Chardon, G.: Réactions vaso-motrices réflexes l'origine aortico-surrénale. *L'Algérie méd.* 55:971, 1951.
- 191 — et Cruck, S.: Influence de l'adrenaline sur la transmission synaptique ganglionnaire. *L'Algérie méd.* 55:973-974, 1951.
- 192 — et Gross, A.: Sur la localisation des synapses sur les voies vaso-motrices extramédullaires de la rate et du rein. *L'Algérie méd.* 55:969-970, 1951.
- 193 —, et Neverre, G.: Localisation de l'action d'un synaptolytique (tétra-éthylbromure d'ammonium) sur le système adrénalino-sécréteur. *Compt. rend. Soc. de biol.* 145:701-704, 1951.
- 194 — et Gross, A.: Action élective de l'ésérine sur les ganglions de plexus coelique. *L'Algérie méd.* 55:974, 1951.
- 195 —, et Neverre, G.: Étude expérimentale chez le chien de l'activité de ganglions du plexus solaire (irrigues in situ). *L'Algérie méd.* 55:970, 1951.
- 196 —, Neverre, G., et Gross, A.: Action de l'ésérine localisée aux ganglions du plexus solaire et à la glande surrenale. *L'Algérie méd.* 55:970-971, 1951.
- 197 Mandl, F.: Observations on reoperation and necropsy after vagotomy. *Wien. klin. Wchnschr.* 62:857-858, 1950.
- 198 —: Der massive Lungenkollaps (Lungenkrampf) nach thorakalen Sympathektomien. *Acta neuroveg.* 2:156-162, 1951.
- 199 —: Das vegetative Nervensystem als Angriffspunkt operativer Eingriffe. *Wien. klin. Wchnschr.* 63:141-144, 161-165, 1951.
- 200 Mark, R. E.: Die Klinik der vegetativen Dystonie. *Wien. klin. Wchnschr.* 63:25-28, 1951.
- 201 —: Das Muskelfibrillieren ein Symptom der vegetativen Dystonie. *Deutsches Arch. f. klin. Med.* 198:383-404, 1951.
- 202 Marley, A. e Soldati, M.: Contributo all' innervazione dell' ovaio: Innervazione delle anastomosi artero-venose. *Boll. Soc. ital. biol. sper.* 27:640-641, 1951.
- 203 Martin, J. K. and Isaac, J. E.: A case of Hirschsprung's disease. *Winnipeg Clin. Quart.* 4:126-133, 1951.
- 204 McDowell, F. H. and Plum, F.: Arterial hypertension associated with acute anterior poliomyelitis. *New England J. Med.* 245:241-245, 1951.
- 205 McCleery, R. S., Kesterson, J. E., and Schaffarzick, W. R.: A clinical study of the effect of vagotomy on recurrent acute pancreatitis. *Surgery.* 30:130-147, 1951.

- ²⁰⁶ McCubbin, J. W. and Page, I. H.: Role of cardioacceleration in chronic experimental neurogenic hypertension. *Am. J. Physiol.* 166:12-14, 1951.
- ²⁰⁷ Mehler, W. R.: An analysis of the lumbar sympathetic trunk in the dog. *Anat. Rec.* 109:65, 1951.
- ²⁰⁸ Meyer, E. R.: Zur Frage der Neurosekretion sympathischer Ganglien und Untersuchungen des Ganglion stellatum bei Tier und Mensch. *Beitr. z. path. Anat.* 111:373-380, 1951.
- ²⁰⁹ Miller, E. M., Knight, A., and Olwin, J. H.: An evaluation of five years' experience with vagotomy in treatment of chronic peptic ulcer. *Arch. Surg.* 63:303-310, 1951.
- ²¹⁰ Mitchell, G. A. G.: The intrinsic renal nerves. *Acta anat.* 13:1-15, 1951.
- ²¹¹ Morton, D. R., Klassen, K. P., and Curtis, G. M.: The clinical physiology of the human bronchi. I. Pain of thoracobronchial origin. *Surgery* 28:699-704, 1950.
- ²¹² Mosinger, M.: Anatomie de l'hypothalamus et du sous-thalamus élargi (Cytoarchitectomie, voies de conduction, histopathologie). *Schweiz Arch. f. Neurol. u. Psychiat.* 65:135-186, 1950.
- ²¹³ Muto, R.: Considerazioni su forma e posizione, rapporti e loggia del ganglio cervicale inferiore nei feti umani. *Boll. Soc. ital. biol. sper.* 27:484-486, 1951.
- ²¹⁴ Nathan, H.: Sympathetic block for preservation of strangulated intestines. *Rev. Gastroenterol.* 18:493-499, 1951.
- ²¹⁵ Nedzel, A. J.: Distribution of chromidia in the sympathetic ganglion cells in man and dogs with hypertension. *J. Neuropath. & Exper. Neurol.* 10:319-324, 1951.
- ²¹⁶ Neil, E.: Chemoreceptor areas and chemoreceptor circulatory reflexes. *Acta physiol. Scandinav.* 22:54-65, 1951.
- ²¹⁷ Neugebauer, J.: Eine neue Methode der Blockade des Halssympathikus. *Zentralbl. Chir.* 76:1010-1014, 1951.
- ²¹⁸ Nicol, J. A. C.: The autonomic nervous system of the Chimaeroid fish. *Hydrolagus collicii*. *Quart. J. Micr. Sc.* 91:379-400, 1951.
- ²¹⁹ Niedermeier, S.: Vasomotorik und Glaukom. *V. Graefe's Arch. f. Ophthalmol.* 151:551-559, 1951.
- ²²⁰ Niedner, F. F.: Beiträge zur Kenntnis von neurovegetativen Lungenreaktionen. *Acta neuroveg.* 1:353-373, 1950.
- ²²¹ Nödl, F.: Über neurogene Nebenzellen in der menschlichen Haut. *Acta neuroveg.* 2:205-209, 1951.
- ²²² Nomura, S.: On the cardiac nerves and ganglia of the mouse. *Cytological and Neurological Studies, U. of Kanazawa.* No. 6:15-40, 1951.
- ²²³ Nosik, W. A.: Stellate ganglion block in cerebro-vascular accidents. *Ann. Int. Med.* 35:409-416, 1951.
- ²²⁴ Nyst, P.: The surgical treatment of bronchial asthma. *Arch. chir. neerl.* 2:261-273, 1950.
- ²²⁵ Oberdahlhoff, H.: Der heutige Stand in der Behandlung des idiopathischen Megacolums im Kindersalter. *Langenbeck's Arch. f. klin. Chir.* 268:45-73, 1951.
- ²²⁶ Oberhelman, H. A., Jr., Woodward, E. R., Smith, C. A., and Dragstedt, L. R.: Effect of sympathectomy on gastric secretion in total pouch dogs. *Am. J. Physiol.* 166:679-685, 1951.
- ²²⁷ Oberholzer, R. J. H.: Responses respiratoires et vasomotrices a la stimulation des nerfs afférents du groupe vagal. *J. de Physiologie.* 43: 329-360, 1951.
- ²²⁸ Obiditsch-Mayer, I.: Veränderungen am neuro-vasculären System der Darmwandt bei chronischer Obstipation. *Langenbeck's Arch. f. klin. Chir.* 268:243-250, 1951.
- ²²⁹ Oliver, J.: Effects of vagus section with subtotal gastrectomy and diversion of

- duodenal secretions into the terminal portion of the ileum on ulcer development. *Arch. Surg.* 62:649-657, 1951.
- ²³⁰ Orahovats, P. D. and Root, W. S.: Effect of total sympathectomy on hemoglobin production in dogs. *Federation Proc.* 10:100, 1951.
- ²³¹ Orkin, L. R., Papper, E. M., and Rovenstine, E. A.: The complications of stellate and thoracic sympathetic nerve blocks. *J. Thoracic Surg.* 20:911-922, 1950.
- ²³² Oremea, F.: Sistema nervoso cerebro-spinale e sistema nervosovegetativo nella patogenesi della sclerodermia diffusa. *Acta neuroveg.* 2:41-73, 1951.
- ²³³ —: Sistema nervoso cerebro-spinale e sistema nervosovegetativo nella patogenesi della sclerodermia diffusa. *Acta neuroveg.* 2:386-407, 1951.
- ²³⁴ Palmer, W. L., Kirsner, J. B., and Levin, E.: An internist views the surgical treatment of peptic ulcer. *J.A.M.A.* 145:1041-1044, 1951.
- ²³⁵ Palumbi, G.: Ulteriori dati sulla innervazione recettrice e vegetativa del labirinto membranoso dell' uomo. *Boll. Soc. ital. biol. sper.* 27:642-643, 1951.
- ²³⁶ Palumbo, L. T.: Sympathectomy in the treatment of Buerger's disease. *Postgrad. Med.* 9:215, 1951.
- ²³⁷ Pansini, A.: L'innervazione vegetativa e sensitiva della pachimeninge encefalica. *Boll. Soc. ital. biol. sper.* 27:486-488, 1951.
- ²³⁸ Peiss, C. N., Hertzman, A. B., and Randall, W. C.: Region rates of cutaneous insensible perspiration. *Federation Proc.* 10:103-104, 1951.
- ²³⁹ Pfeffer, K. H.: Vegetative Fehlregulationen mit tödlichem Ausgang nach Sympathektomie bei Hypertonikern. *Ztschr. klin. Med.* 148:380-395, 1951.
- ²⁴⁰ Picard, H.: Intrathoracic endoscopic exeresis of splanchnic nerve in patients with gastroduodenal ulcer. *Schweiz. med. Wchnschr.* 81:250-254, 1951.
- ²⁴¹ —: Intrathorakale endoskopische Splanchnicusexärese bei Magen-Duodenal-Ulcus. *Schweiz. med. Wchnschr.* 81:250-252, 1951.
- ²⁴² Piccinno, A.: Sulla fine innervazione della vescica umana. *Boll. Soc. ital. biol. sper.* 27:238-239, 1951.
- ²⁴³ Pichler, E.: Vegetative Schmerzbeämpfung der Neuritis. *Wien. klin. Wchnschr.* 63:279-281, 1951.
- ²⁴⁴ Pick, J. and Sheehan, D.: Sympathetic rami in the frog. *Anat. Rec.* 109:77, 1951.
- ²⁴⁵ Polley, E. H.: An analysis of the nerves along blood vessels in skin and striated muscle of the hindlimb of the cat. *Anat. Rec.* 109:78, 1951.
- ²⁴⁶ Pollock, L. J., Boshes, B., Chor, H., Finkelman, I., Arieff, A. J., and Brown, M.: Defects in regulatory mechanisms of autonomic functions in injuries of spinal cord. *J. Neurophysiol.* 14:85-93, 1951.
- ²⁴⁷ Pötzl, O.: Leukotomie und Vegetativum. *Acta neuroveg.* 1:317-341, 1951.
- ²⁴⁸ Pratt, G. H.: Surgical management of the postthrombotic syndrome, with reference to the use of sympathectomy. *Am. J. Surg.* 81:562-567, 1951.
- ²⁴⁹ Pribor, H. C.: Innervation of the uterus. *Anat. Rec.* 109:79, 1951.
- ²⁵⁰ Randall, W. C., Hertzman, A. B., and Ederstrom, H. E.: Dermatomeal recruitment of sweating in response to heat. *Federation Proc.* 10:108, 1951.
- ²⁵¹ Rapaport, S. I., Frank, H. A., and Massell, T. B.: The effect of smoking upon blood flow in a sympathectomized limb. *Circulation.* 2:850-858, 1950.
- ²⁵² Reed, A. F.: The origins of the splanchnic nerves. *Anat. Rec.* 109:81, 1951.
- ²⁵³ Reeve, E. B., Nanson, E. M., and Rundle, F. F.: Observations on inhibitory respiratory reflexes during abdominal surgery. *Clin. Sci.* 10:65-87, 1951.
- ²⁵⁴ Reid, L. C.: Practical considerations in the surgical management of children with regard to the autonomic nervous system. *New York State J. Med.* 50:2937-2939, 1950.

- ²⁵⁵ Rickenbach, K. and Mussen, H.: Vergleichende reizphysiologische und anatomische Untersuchungen der reflektorischen Atemzentren der Medulla Oblongata des Kaninchens. *Acta anat.* 12:135-173, 1951.
- ²⁵⁶ Robertson, C. W. and Smithwick, R. H.: The recurrence of vasoconstrictor activity from limb sympathectomy in Raynaud's disease and allied vasomotor states. *New England J. Med.* 245:317-320, 1951.
- ²⁵⁷ Ross, J. R. and Broisma, M. P.: Splanchnicectomy: its clinical effects on the gastro-intestinal tract. *Gastroenterology.* 17:389-399, 1951.
- ²⁵⁸ Safley, T. J.: Painful lesions of the upper extremity treated by injecting the stellate ganglion with procaine hydrochloride. *Mississippi Doctor.* 28:402-405, 1951.
- ²⁵⁹ Sähloff, O.: Die Behandlung vegetativ bedingter Beschwerden der Frau insbesondere der prämenstruellen Beschwerden und der Dysmenorrhoe. *Med. Klin.* 32:866-868, 1951.
- ²⁶⁰ Sakamoto, K.: Histological study on the innervation of the human cornea. *Tohoku J. Exper. Med.* 54:105-114, 1951.
- ²⁶¹ Sanders, R. L.: Technic of transabdominal vagotomy. *Am. J. Surg.* 81:573-576, 1951.
- ²⁶² Sandri, B.: Das vegetative Nervensystem und die Currysche Arantheorie. *Deutsche med. Wchnschr.* 76:46-47, 1951.
- ²⁶³ Sautter, H. and Hager, H.: Vom Einfluss des vegetativen Systems auf das Wachstum der Geschwülste, speziell der Melanoblastome. *Graefe's Arch. f. Ophth. & Arch. f. Aughk.* 151:156-166, 1950.
- ²⁶⁴ Schuetz, H.: Die vegetativ nervöse Beeinflussung der Pankreassekretion. *Wien. klin. Wchnschr.* 63:180-182, 1951.
- ²⁶⁵ Schölmerich, P. und Hildebrandt, G.: Ueber Mechanismus und Regulation der Hautwassersabgabe. *Ztschr. ges. exper. Med.* 117:17-36, 1951.
- ²⁶⁶ Scholz, W.: Über die Wertigkeit der Symptome der vegetativen Dystonie. *Acta neuroveg.* 2:329-356, 1951.
- ²⁶⁷ Schönbrunner, E.: Die Hypoxämie des Herzmuskels und deren Beziehung zum vegetativen Nervensystem. *Acta neuroveg.* 2:171-188, 1951.
- ²⁶⁸ Schroeder, W. und Anschutz, H. F.: Die Wirkung von Azetylcholin, Adrenalin und Histamin auf die Durchblutung der Kapillaren und arteriovenösen Anastomosen in der vorderen Extremität des Hundes. *Ztschr. f. Biol.* 103:395-408, 1950.
- ²⁶⁹ —: Der Einfluss der Narkose auf die Funktion vegetativer Reflexe. *Ztschr. ges. exper. Med.* 117:37-48, 1951.
- ²⁷⁰ Shafer, P. W. and Kittle, C. F.: The relation of the autonomic nervous system to gastric secretion with particular reference to the sympathetic nerves. *Surgery.* 29:1-10, 1951.
- ²⁷¹ Shepherd, J. T.: Evaluation of treatment in intermittent claudication. *Brit. M. J.* 1413-1418, 1950.
- ²⁷² —: The effect of acute occlusion of the femoral artery on the blood supply to the calf of the leg before and after release of sympathetic vasomotor tone. *Clin. Sci.* 9:355-365, 1950.
- ²⁷³ Shieh, P.: The neof ormation of cells of preganglionic type in the cervical spinal cord of the chick embryo following its transplantation to the thoracic level. *J. Exper. Zool.* 117:359-395, 1951.
- ²⁷⁴ Siedek, H.: Das vegetative System und pathologische Kreislaufreaktionen. *Wien. klin. Wchnschr.* 63:157-161, 1951.
- ²⁷⁵ Simeone, F. A., Mentha, C., and Rodrigues, H. A.: Responsiveness of sweat glands

- after denervation by preganglionic ramisection, ganglionectomy and peripheral nerve section. *Am. J. Physiol.* 165:356-364, 1951.
- 276 Sinclair, J. G.: A ganglionic plexus in the human falx cerebri. *Texas Rep. Biol. & Med.* 9:348-352, 1951.
- 277 Smets, W. et Xhigne, M.: La gastrectomie d'emblée dans les perforations aiguës d'ulcères gastro-duodénaux. *Acta chir. belg.* 50:305, 1951.
- 278 Smith, D. W.: Stellate ganglion block: the tissue displacement method. *Am. J. Surg.* 82:344-348, 1951.
- 279 — and Larkin, M. A.: The surgical significance of the cardiosplanchnic reflex. *South. M. J.* 44:399-407, *Abs. Int. Surg. Dig.* 52:106-109, 1951.
- 280 Sonnenschein, R. R., Kobrin, H., Janowitz, H. D., and Grossman, M. I.: Stimulation and inhibition of human sweat glands by intradermal sympathomimetic agents. *J. Appl. Physiol.* 3:573-581, 1951.
- 281 State, D. and Rogers, W.: The surgical treatment of idiopathic congenital megacolon. *Bull. Univ. Minnesota Hospitals & Minnesota Med. Foundation.* 22:164-168, 1950.
- 282 Stein, I. F., Jr., Grossman, M. I., Meyer, K. A., and Ivy, A. C.: Physiologic rationale for the surgical treatment of peptic ulcer. *Surg., Gynec. & Obst.* 92:110-112, 1951.
- 283 Stevens, G. A., Kipen, C. S., and Ross, W. L.: Surgical treatment of duodenal ulcer. *Ann. Western Med. & Surg.* 5:275-278, 1951.
- 284 Sturm, A.: Aktuelle neurovegetative Probleme. *Deutsche med. Wchnschr.* 76:449-453, and 76:543-547, 1951.
- 285 Sussman, I., Lempke, R., and Wallace, R.: Stellate ganglion block in cerebral thrombosis and embolism. *Am. Pract. & Dig. of Treat.* 2:217-220, 1951.
- 286 Swenson, O., Segnitz, R. H., and Shedd, R. H.: Hirschsprung's disease. New surgical treatment. *Am. J. Surg.* 81:341-347, 1951.
- 287 Tinkel, H. I.: A case of gustatory sweating. *J. Neurol., Neurosurg. & Psychiat.* 14:129-133, 1951.
- 288 Taylor, A. C. and Butcher, E. O.: The regulation of eruption rate in the incisor teeth of the white rat. *J. Exper. Zool.* 117:165-188, 1951.
- 289 Taylor, J. R.: The physiology of micturition in normal and neurogenic bladders. *Winnipeg Clin. Quart.* 4:115-125, 1951.
- 290 Taylor, R. D., Page, I. H., and Corcoran, A. C.: Hormonal neurogenic vasopressor mechanisms. *Arch. Int. Med.* 88:1-9, 1951.
- 291 Tchong, K. T.: Innervation of the dog's heart. *Am. Heart J.* 41:512-522, 1951.
- 292 —: Synapses interneuronales dans les ganglions cardiaques. *Acta anat.* 11:431-443, 1951.
- 293 Terzuolo, C.: Ricerche sul ganglio ciliare degli uccelli. Connessioni, mutamenti in relazione all'età e dopo recisione delle fibre pregangliari. *Ztschr. Zellforsch.* 36:255-267, 1951.
- 294 Thalhammer, O. und Janicek, L.: Die unspezifische Therapie (Chorea minor) im Lichte einer neuen vegetativ-regulatorischen Leukozytenreaktion. *Wien. klin. Wchnschr.* 63:198-200, 1951.
- 295 Thomas, J. E.: Myenteric reflex in dog's duodenum. *Federation Proc.* 10:136, 1951.
- 296 Thorek, P.: Vagotomy for idiopathic ulcerative colitis and regional enteritis. Results in twenty-one cases. *J.A.M.A.* 145:140-146, 1951.
- 297 Truex, R. C.: Chromaffin tissue of the sympathetic ganglia and heart. *Anat. Rec.* 108:687-697, 1950.

- 298 —: The sympathetic ganglions of hypertensive patients. *Arch. Path.* 51:186-191, 1951.
- 299 Tum Suden, C. and Marazzi, A. S.: Synaptic inhibitory action of adrenaline at parasympathetic synapses. *Federation Proc.* 10:138, 1951.
- 300 Uebenhör, R.: Die Nerven der Blase nach klinischen Erfahrungen. *Wien. klin. Wchnschr.* 63:202-204, 1951.
- 301 Van Dobben-Broekema, M. and Dirken, M. N.: Reactions of the vessels of the rabbit's ear in response to heating the body. *Acta physiol. et pharmacol. neerl.* 1:562-583, 1950.
- 302 —: Influence of the sympathetic nervous system on the circulation in the rabbit's ear. *Acta physiol. et pharmacol. neerl.* 1:584-602, 1950.
- 303 Van Liere, E. J., Hess, H. H., and Fedor, E. J.: Effect of painful stimuli on intestinal motility of albino and hooded rats. *Federation Proc.* 10:139, 1951.
- 304 Von Euler, U. S.: Hormones of the sympathetic nervous system and the adrenal medulla. *Brit. M. J.* 1:105-108, 1951.
- 305 —: The nature of adrenergic nerve mediators. *Pharmacol. Rev.* 3:247-277, 1951.
- 306 Wachholder, K. and Neuberg, H. J.: Ueber den Einfluss des vegetativen Nervensystems auf das weisse Blutbild nach Untersuchungen am Ebbeckeschen Eintauchreflex. *Arch. ges. Physiol.* 253:91, 1950.
- 307 Wada, T. and Kurosawa, K.: Dorsomedial thalotomy III: Influence upon function of autonomic nervous system. *Tohoku J. Exper. Med.* 54:237-238, 1951.
- 308 Wall, P. D. and Davis, G. D.: Three cerebral cortical systems affecting autonomic function. *J. Neurophysiol.* 14:507-517, 1951.
- 309 Walters, W. and Belding, H. H.: Physiological effects of vagotomy. *J.A.M.A.* 145:607-613, 1951.
- 310 —, et Lillie, W. I.: Vagotomie gastrique. *Lyon chir.* 46:775-783, 1951.
- 311 —, and Hoon, J. R.: Vagotomy and subtotal gastric resection with vagotomy in cases of gastrojejunal ulcers and fistulas after multiple previous surgical procedures. *J. Mt. Sinai Hosp.* 17:423-428, 1951.
- 312 Watzka, M. and Scharf, J. H.: Die Paraganglien am Ganglion nodosum vagi und dessen Umgebung beim Erwachsenen Menschen. *Ztschr. Zellforsch. u. mikr. Anat.* 36:141-150, 1951.
- 313 Wetherell, F. S.: Resection of the superior hypogastric plexus. Modification of the technic to prevent regeneration. *Am. J. Obst. & Gynec.* 61:738-742, 1951.
- 314 Whitelaw, G. P. and Smithwick, R. H.: Effect of extensive sympathectomy upon blood pressure responses and levels. *Angiology.* 2:157-172, 1951.
- 315 Wilde, F. R.: The perivascular neural pattern of the femoral region. *Brit. J. Surg.* 39:97-105, 1951.
- 316 Williams, H. L.: A concept of allergy as autonomic dysfunction suggested as an improved working hypothesis. *Tr. Am. Acad. Ophth. & Otol.* 55:123-146, 1950.
- 317 —: A concept of allergy as autonomic dysfunction suggested as an improved working hypothesis. *Ann. Otol. Rhin. & Laryng.* 60:122-151, 1951.
- 318 Wilson, M.: Observations on the extent of denervation after thoracic and thoracolumbar sympathectomy. *Proc. Roy. Soc. Med.* 43:1065-1068, 1950.
- 319 Woldring, S. and Dirken, M. N. J.: Site and extension of bulbar respiratory centre. *J. Neurophysiol.* 14:227-241, 1951.
- 320 Wolferth, C. C., Jeffers, W. A., Lukens, F. D. W., Zintel, H. A., and Hafkenschiel, J. H.: Observations on the results of subtotal adrenalectomy in the treatment of severe, otherwise intractable hypertension and their bearing on the mechanism by which hypertension is maintained. *Ann. Int. Med.* 35: 8-18, 1951.

- 321 Wrete, M.: Variation of silver impregnation in different systems of nerve fibers. *Acta anat.* 12:198-206, 1951.
- 322 —: Ganglia of rami communicantes in man and mammals particularly monkey. *Acta anat.* 13:329-336, 1951.
- 323 Youmans, W. B.: Adrenergic blocking agents as diagnostic aids in arterial hypertension. *Ann. Western Med. & Surg.* 5:687-696, 1951.
- 324 Zimmermann, J.: Ganglioneuroblastom als erbliche Systemerkrankung des Sympathicus. *Beitr. Z. pathol. Anat.* 111:355-372, 1951.
- 325 Bange, W.: Stellatumblockade und Pneumothorax. *Med. Klin.* 45:1175-1178, 1951.
- 326 Benjamin, H. B.: The neurovascular mechanism of the mucous membrane of the stomach. *Surg. Gynec. & Obst.* 93: 672-675, 1951.
- 327 Bonvallet, M., Morel, E., et Benda, P.: Sur la mécanique de la transmission à l'hypophyse des stimuli provoquant la décharge émotionnelle d'hormone corticotrope, chez le chien. *Compt. rend. Soc. biol.* 145:1055-1060, 1951.
- 328 Braeucker, W.: Die konservative Neuraltherapie am Kopf. *Acta neuroveg.* 3:246-252, 1951.
- 329 Brooker, R. M.: Anatomic studies on the sympathetic nervous system. *Arch. Surg.* 63:799-806, 1951.
- 330 Blanchon, P.: Que peut-on attendre des interventions chirurgicales sur le système nerveux autonome au cours de l'asthme? *La Revue du Practicien (Suppl.)* No. 5:139-143, 1951.
- 331 Burger, M.: Diencephalon als psychosomatische Schaltstelle. *Acta neuroveg.* 3:120-131, 1951.
- 332 Dittmar, F.: Der kutiviscerale Reflex. *Acta neuroveg.* 3:236-245, 1951.
- 333 Duff, R. S.: Circulatory changes in the forearm following sympathectomy. *Clin. Sci.* 10:529-540, 1951.
- 334 Euler, C. von: Potentialverschiebungen in vegetativen Zentren. *Acta neuroveg.* 3:113-119, 1951.
- 335 Gobel, P. und Fischer, H.: Untersuchungen von 24-Stunden-Schwankungen verschiedener Körperfunktionen. Ein Beitrag zur Analyse vegetativer Regulationsstörungen. *Deutsches Arch. f. klin. Medizin.* 198:600-611, 1951.
- 336 Gohrbandt, E.: Die Behandlung der multiplen Sklerose durch Novocainblockade des Sympathicus. *Langenbeck. Arch. u. Dtsch. Z. Chir.* 270:295-299, 1951.
- 337 Gross, D.: Die vasale (arterielle) Ordnung der Körperoberfläche und was sie bedeutet. *Acta neuroveg.* 3:171-197, 1951.
- 338 Hagen, E.: Neurohistologische Beobachtungen an Hypophyse und Zwischenhirn des Menschen. *Acta neuroveg.* 3:67-76, 1951.
- 339 Hild, W.: Das Verhalten des neurosekretorischen Systems nach Hypophysenstieldurchschneidung und die physiologische Bedeutung des Neurosekrets. *Acta neuroveg.* 3:81-112, 1951.
- 340 Hilger, J. A.: Autonomic dysfunction in otolaryngology. *Tr. Am. Acad. Ophth.* 56: 716-723, 1951.
- 341 Kaiser, F., Reich, E., und Sarre, H.: Klinische Erfahrungen mit einem neuen ganglienblockierenden Mittel. *Deutsche med. Wchnschr.* 76:1443-1448, 1951.
- 342 Llaverio, F.: Die Stellung des Zwischenhirnsystem, seine funktionelle Grenze und seine Bedeutung besonders für die endogene Psychose. *Acta neuroveg.* 3:253-266, 1951.
- 343 Mohamed, M. S. and Bean, J. W.: Local and general alterations of blood CO₂ and influence of intestinal motility in regulation of intestinal blood flow. *Am. J. Physiol.* 167:413-425, 1951.

- ³⁴⁴ Oberholzer, R. J. H.: Réponses respiratoires et vasomotrices a la stimulation des nerfs afférentes du groupe vagal. *J. de physiol.* 43:329-360, 1951.
- ³⁴⁵ Orthner, H.: Anatomische Befunde im Hypophysen-Hypothalamus-System bei Fehlen der intrasellären Hypophyse und bei Kastration. *Acta neuroveg.* 3:50-53, 1951.
- ³⁴⁶ Ortman, R.: Ueber morphologisch-experimentelle Veränderungen am Hypothalamo-Hypophysensystem. *Acta neuroveg.* 3:80, 1951.
- ³⁴⁷ Raab, W.: Ueber eine sympathikomimetische Substanz im Gehirn. *Acta neuroveg.* 3:77-79, 1951.
- ³⁴⁸ Scott, J. C. and Reed, E. A.: Electrocardiographic effects of reflex vagal stimulation. *Am. J. Physiol.* 167:441-449, 1951.
- ³⁴⁹ Schumacker, H. B.: Sympathectomy in the treatment of frostbite. *Surg. Gynec. Obst.* 93:727-734, 1951.
- ³⁵⁰ Smith, S. W.: The correspondence between hypothalamic neurosecretory material and neurohypophyseal material in vertebrates. *Am. J. Anat.* 89:195-233, 1951.
- ³⁵¹ Spatz, H.: Neues über die Verknüpfung von Hypophyse und Hypothalamus. *Acta neuroveg.* 3:5-49, 1951.
- ³⁵² Stern, P.: Muskelerkrankungen und neurovegetatives System. *Acta neuroveg.* 3:211-216, 1951.
- ³⁵³ Sturm, A.: Das Metamerie-Problem in der inneren Medizin. *Acta neuroveg.* 3:132-153, 1951.
- ³⁵⁴ Wildi, E.: Noyaux tubériens et noyaux magnocellulaires hypothalamiques d'un idiot microcéphale hypogénital. *Acta neuroveg.* 3:54-66, 1951.
- ³⁵⁵ Zenker, R. und Löhr, H. H.: Die Ergebnisse der Sympathektomie beim Hochdruck. Langenbeck. *Arch. u. deutsch. Ztschr. f. Chir.* 270:277-284, 1951.

Neuro-Endocrine Relationships

By RACHMIEL LEVINE, M.D. AND MAURICE S. GOLDSTEIN, M.D.

THE collection of neurones and of modified secretory nerve cells which constitutes the hypothalamic region, is, despite its small size, the meeting ground of neurologic, metabolic and endocrine control systems. The mass of material concerning the functions of the hypothalamus is continually increasing without, as yet, giving evidence of the possibility of an integrating viewpoint. We have selected some of the new material on the subject for more extended comment.

Work which was initiated by Hetherington and Ranson and continued by Brobeck, Brooks, and others, showed some years ago that discrete bilateral lesions placed at the edges of the ventromedial nuclei and lateral to them, result in continuing hyperphagia and, consequent, obesity. The increased appetite began immediately postoperatively and continued indefinitely. Hypophysectomy, prior to the electrolytic lesion, did not interfere with the appearance or degree of hyperphagia. Thus, neither the pituitary hormones nor the glands controlled by the hypophysis intervene in the hypothalamic type of obesity. Since the destruction of the area indicated above led to hyperphagia, the undisturbed function of that area in vivo must be one of inhibiting food intake. Very recently, Anand and Brobeck⁵ showed that in rats, as well as in cats, the bilateral electrolytic destruction of areas immediately outside this appetite inhibiting center, and extending laterally to the edge of the hypothalamus, lead to immediate and continuing inhibition of appetite. The animals die of inanition in the midst of plenty. In vivo then, this region must be the food intake promoting area. Together, these two adjacent centers form a balanced control system. Last year, from the same laboratory, Stevenson showed the existence of a hypothalamic mechanism for the adjustment of the proper intake of water in relation to the solids in the food.

It is not known whether these regulatory systems exert their effects upon the internal viscera (g.i. tract) or upon the higher cortical centers. A suggestion has been made that the hyperphagia may not be an increased desire for food, but rather an inability to know when to stop. Despite these shortcomings in our knowledge of mechanisms at this level, these

centers provide at least an anatomic locale for the expression of such disorders as anorexia nervosa, bulimia and perhaps certain cases of obesity.

In 1932, the observation was made by Schittenhelm and Eisler that certain areas in the midbrain and tuber cinereum showed iodine accumulation. This could be demonstrated only when the thyroid was present. A school of European physiologists and clinicians pointed to this fact as partial evidence for the belief that the thyroid hormone acted primarily upon the vegetative centers, the heightened activity of which produced many of the signs and symptoms of hyperthyroidism. This view did not prove fruitful, although it is not completely without foundation. Jensen and Clark⁹ have recently demonstrated that radioactive inorganic iodine administered to hypothyroid rabbits does not tend to accumulate in any specific locality of the midbrain. However, radioactively labelled thyroxine accumulates in the neurohypophysis, infundibulum, tuber cinereum, and median eminence. There is less accumulation in the anterior hypophysis. These studies substantiate the older reports but do not by themselves provide an indication of a possible function of thyroxine localization in this area. One possible function is suggested by the work of Greer⁷ on the hypothalamic control of the pituitary release of thyrotropin. Greer produced bilateral lesions extending from behind the supraoptic nuclei to the caudal part of the ventromedial nuclei in rats. Three weeks postoperatively, the animals were placed on a diet containing propylthiouracil. This drug, of course, inhibits the synthesis of thyroxine which, in turn, leads to a low thyroxine level in the circulating blood. This thyroxine deficiency stimulates the output of thyrotropin from the pituitary. The thyroid gland, consequently, becomes hyperplastic even though it is hormonally inactive. In the rats operated upon by Greer, the thyroid glands did not become hyperplastic. That is, thyrotropin was not released in adequate amounts despite evidence of a low synthesis of thyroxine. In these animals, the pituitary glands were anatomically intact and were presumably capable of elaborating thyrotropin. This work, taken in conjunction with the localization of radio-thyroxine discussed above, suggests that the thyroxine level of certain hypothalamic areas may be the factor controlling thyrotropin release and, therefore, thyroid function.

Additional work by Sawyer, Markee and Everett^{10, 11} has substantiated their earlier reports on the neuro-humoral control of ovulation. Banthine, which primarily inhibits cholinergic activity, can block ovulation if applied promptly following the initiating reflex stimulus. Inhibitors of the sympathetic system will block the final release of lutenizing hormone even if applied as long as one hour after the initiation of the reflex. All blocking agents fail to prevent the ovulation due to the direct action of injected gonadotropins upon the ovary. The agents, therefore, act upon neural

stations of excitation preceding the release of lutenizing hormone from the pituitary.

Much of our knowledge concerning the hypothalamic-pituitary relations are derived from the consequences of section of the pituitary stalk. Through the work of Harris and others, it has come to be regarded that the pituitary stalk section interrupted a humoral pathway via the blood flow in the hypophysial portal vessels. Greep and Barnett⁸ have done careful stalk sections in rats and have observed the resulting depressed activity of the pituitary target glands. However, they have also made a careful study of the effects of their stalk section upon the histology of the severed anterior pituitary. From their study, it appears that stalk section may damage the blood supply to the pituitary itself, sufficiently to account for depressed function without invoking hypothalamic trophic control of the hypophysis. This work does not disprove neuro-humoral control, but it makes interpretation of the work of many authors more difficult and introduces the need for more caution in interpretation.

The comparatively large doses of ACTH and cortisone which are used for the alleviation of symptoms of many inflammatory disorders, exert certain effects upon the central nervous system. Among these are heightened psychomotor activity (euphoria), an occasional acute psychotic episode, poorly understood EEG changes, an increase in appetite and a decreased reactivity to the production of fever. The underlying mechanisms on which the hormones act are completely unknown. Alman and Fazekas¹ tested the notion that the ACTH effects on brain may perhaps be reflected in an increased oxygen consumption of the organ. No significant changes were seen in blood flow, resistance of the vascular bed or oxygen consumption of the brain in patients undergoing therapy for collagen diseases who received large doses of ACTH.

Previous observations had shown that the EEG of patients with Addison's disease tend to be abnormal and that DCA therapy would not restore the normal pattern. Cortisone, however, led to such a restoration. Bergen⁶ found slowing of wave frequency in adrenalectomized rats which was also not restored by DCA, but became normal after the administration of adrenal cortical extract or $\Delta 5$ -pregnenalone.

Altschule et al.²⁻⁴ have reported further work on changes in the indices of adrenal cortical function of psychotics before and after electroshock therapy. The authors conclude that their present data support their thesis that the psychotic has a heightened adrenal cortical reactivity in respect to certain metabolic functions, and that an induced remission is accompanied by a depression of these same activities. On the basis of available knowledge, it is difficult to prove or disprove this thesis.

REFERENCES

- ¹ Alman, R. W. and Fazekas, J. F.: Effects of ACTH on cerebral blood flow and oxygen consumption. *Arch Neurol. & Psychiat.* 65:680-682, 1951.
- ² Altschule, M. D. and Parkhurst, B. H.: Effect of treatment on excretion of 17-ketosteroids in patients with mental disease. *Arch. Neurol. & Psychiat.* 64:516-527, 1950.
- ³ —, Promisel, E., Parkhurst, B. H., and Grunebaum, H.: Effects of ACTH in patients with mental disease. *Arch. Neurol. & Psychiat.* 64:641-649, 1950.
- ⁴ —, Seigel, E., and Mora-Castaneda, F.: Significance of rise in blood sugar level after injection of epinephrine in mental disease. *Arch. Neurol. & Psychiat.* 65:589-592, 1951.
- ⁵ Anand, B. K. and Brobeck, J. R.: Hypothalamic control of food intake in rats and cats. *Yale J. Biol. & Med.* 24:123-129, 1952.
- ⁶ Bergen, J. R.: Rat electrocorticogram in relation to adrenal cortical function. *Am. J. Physiol.* 164:16-22, 1951.
- ⁷ Greer, M. A.: Evidence of hypothalamic control of the pituitary release of thyrotropin. *Proc. Soc. Exper. Biol. & Med.* 77:603-608, 1951.
- ⁸ Greep, R. O. and Barnett, R. J.: The effect of pituitary stalk-section on the reproductive organs of female rats. *Endocrinology.* 49:172-183, 1951.
- ⁹ Jensen, J. M. and Clark, D. E.: Localization of radioactive 1-thyroxine in the neurohypophysis. *J. Lab. & Clin. Med.* 38:663-670, 1951.
- ¹⁰ Sawyer, H., Markee, J. E., and Everett, J. W.: Blockade of neurogenic stimulation of the rabbit adenohypophysis by banthine. *Am. J. Physiol.* 166:223-228, 1951.
- ¹¹ —: Failure of nerve blocking agents to prevent the effects of placental gonadotrophins in the rabbit. *Endocrinology.* 49:162-167, 1951.

Electroencephalography

By MARY A. B. BRAZIER, B.Sc., PH.D.

IF ONE may hazard a prediction, last year may prove to have been a most productive one for electroencephalography. There have been no large Congresses to draw people from their clinics and laboratories and fewer papers have been published. Therefore, why not infer that more work has been done?

Last year's publications have been helpfully summarized,^{58, 101} and a general discussion has been published.¹⁶⁵ Two symposia are now in print, both of which deal with the organization of cerebral mechanisms.^{28, 107} No electroencephalographer who is concerned with the implications of the information derived by his technics can afford to miss these discussions.

A thoughtful essay on the various theories advanced to explain the nature of the EEG has been written by Wyss.¹⁷¹ He rejects the hypotheses that the waves are envelopes of spikes; that they are the direct result of centripetal impulses; that they are caused by reverberation in closed circuits; that synaptic transmission is responsible for the timing of the rhythm. He gives his allegiance to the concept of an autorhythmicity of the somato-dendritic potentials of cortical cells maintained by metabolic processes and synchronized by the electrical fields of the active neurones themselves. He emphasizes that these are local processes and not propagated potentials. The question of motility of cell parts is not discussed.

Eccles,⁵¹ on the other hand, makes a different interpretation, basing his argument on the premise that the responses of neurones have essentially the same characteristics anywhere in the central nervous system. Paying due regard to the orientation of cell structures in the cortex, he supports Burns²⁷ in the thesis that 'spontaneous' cortical rhythms derive from activity in neuronal chains and not from any inherent rhythmicity of individual neurones. The schema he suggests would encompass not only Burns²⁷ finding of electrical silence in the unanesthetized cortex when completely isolated from the rest of the nervous system, but also the superficial negative response obtained by Adrian on stimulation of the cortical surface, a phenomenon investigated further this year by Burns²⁷ and by Chang.^{29, 30} Eccles regards this as the synaptic potential of apical

pyramidal dendrites excited by spread of discharge in the axons of the superficial layer of horizontal cells. With stronger stimulation a surface positive response follows the initial negative one as the excitation spreads to deeper layers.

Lilly's technic^{104, 105} of 25 electrodes implanted within a space of 0.64 sq. cm. of cortex is giving a type of information about the character of 'spontaneous' activity and evoked responses in the auditory area that has not been available before. Measurements have been made of the speed of the travelling waves. This is one of the most promising of the new approaches to this problem.

Another method which brings us finer resolution in our search for signals of low voltage (evoked responses) hidden among noise of higher amplitude (the background EEG) is the use of an electronic correlator. A description of the application of this technic to electroencephalography was given by Brazier and Casby²⁴ at a meeting of the Eastern Association of EEG. Further work on its use for the detection among other EEG potentials of specific responses (to light and to sound) is in progress.

Yet another method for detection of time-locked evoked responses is available to users of automatic frequency analyzers of the Walter type (Casby). By very narrow tuning of the resonating circuits which correspond to the frequency of the stimulus and to its harmonics (so that the die-away time for each is very long), responses of the cortex at these frequencies will stand out from the background EEG. The resonating circuits (without integration) assigned this task write their information independently on the record through the standard pens of the inkwriting electroencephalograph. If phase is rigidly controlled, a reasonable replica of the response can be reconstructed from addition of the harmonics. This modification of the technic in some degree anticipates suggestions made in the critique presented by Vogel¹⁶² at the Marseilles Symposium.

A technic for detecting the presence of a recurrent response in the EEG has been published by G. Dawson.⁴¹ This, although it does not give information on the phase of each component frequency as does the electronic correlator, is an improvement over the method of superimposed sweeps in that a summation technic is used, i.e., the records are added automatically to obtain the mean. A regularly recurring response will in this way give a mean standing clearly above that of the random background activity.

The study of evoked responses in the animal and in man, both with and without metrazol, has this year engrossed more workers than any other single facet of EEG. The wide use of photic stimulation in clinical work has directed attention to the detailed character of the responses to light not only at the cortex, but along the optic pathway.⁶⁰ Some clue as to the neurones immediately responsible for the several components of the cortical

response to light may come from the work in progress on their relation to maturation of these neurones in infant animals (Hunt and Goldring).⁸¹ More evidence has been gathered that the response to flicker is not a driving of the alpha rhythm.^{25, 124} All workers do not differentiate clearly between evoked responses and "driving." Fundamental for the understanding of the evoked response at the visual cortex is the paper by Bishop and Clare¹⁸ whose analysis shows that there is only one spike in the optic radiation on single shock stimulation of the optic nerve although there are three (or more) in the cortex, these others being contributed by wholly intracortical neurones, cells in other cortical layers being responsible for the subsequent slow waves.¹⁸ This interpretation (supported by the observation of Marshall¹¹² that all components except the first spike are affected by spreading depression) differs from that of Chang who has postulated that the three spikes evoked at the cortex by a single volley to the nerve may indicate three fiber sizes, and consequently three conduction rates, in the optic radiation. This is a field where orientation of electrodes within the three dimensions of the brain is indeed critical. The detection of phase reversals as the exploring electrode penetrates succeeding layers of the cortex is invaluable in locating electrical events due to intracortical discharges, and is now used by many workers.^{6, 18, 147} Caution should, however, be used when the exploring electrode may be in a sulcus.

Bremer²⁶ has been able to analyze evoked responses at the cerebellar cortex and finds, after the initial positive wave, a negative spike associated with discharge of the Purkinje cells. A slower negative wave follows, and would appear to represent temporally dispersed efferent discharges. He has also demonstrated a remarkable convergence of afferent systems in the cerebellar cortex so that response to one type of sensory stimulation can inhibit response to another.^{26a}

One of the most striking reports on cortical concomitants is Bates'¹² demonstration that the onset of a voluntary movement coincides with a certain phase of the alpha rhythm. If photographs of several records are superimposed it is found that for a period of approximately half a second before each voluntary movement of the hand is made, the alpha waves are locked in similar phase. This does not occur when the same movement is involuntarily induced (by stimulation). Shunning the question of the neurophysiology lying behind the word "voluntary," other than that it implies the inclusion of the brain in the circuit, one may observe that here are data that need to be considered in any hypothesis framed to explain the alpha rhythm.

Dell^{47, 48} has traced the thalamic, cortical and cerebellar representation of the vagus; a primary response at the insular cortex follows 8 to 10 seconds

after a stimulus to the end of the vagus cut at the neck. To obtain secondary responses he found frequency of stimulation to be critical and traced them in mesencephalic nuclei, thalamus, hypothalamus and in the amygaloid complex.

There is a growing interest in the responses (electrocortical, autonomic and behavioral) to electrical stimulation of various parts of the rhinencephalon, and the effects also of its fractional ablation. For a comprehensive review of previous work on animals, together with considerable new material, the reader is recommended to consult the monograph by Kaada.⁸⁹ In man, studies have been made of autonomic responses during stimulation of the cingulate gyrus and uncus as well as the anterior temporal and orbital cortices by several workers;^{102, 103, 132, 145} the uncus effects are the more striking.^{103, 145} M. Lennox,⁹⁹ from her results on anterior cingulate stimulation in animals, suggests a possible relation with the mechanism operating in petit mal epilepsy. Stoll¹⁵² has published electrophysiologic studies of the subcortical connections of the anterior temporal region in the cat.

A most interesting discussion of the possible mechanisms acting in an epileptic seizure was given by Jung⁸⁷ at the Geneva Symposium. In fits induced in animals by electrical stimulation the spike at the site of excitation is followed by a slow wave of long duration and later by trains of normal waves which Jung suggests are the expression of an equilibrating mechanism for restoring the cortex to its normal level. Just before a seizure, these later potentials are depressed (as though the restraining mechanism had failed). The same author has also made a study of the pathways of propagation of discharges in the various phases of a convulsion.

EEG responses to sound during sleep have been recorded by Pas-souant^{125, 126} in epileptics. An apparent recruitment of response follows slowly repeated stimuli (10 to 15 per minute); in non-focal epilepsy, the resultant discharges are generalized but in focal epilepsy they are asymmetrical (with the exception of cases with unilateral temporal lobe foci which on auditory stimulation discharge bilaterally).

Gibbs⁶⁵ has described a type of spike discharge which he found in eight out of 300 control subjects and 312 out of 5000 epileptics. He describes these as 14 per second and 6 per second positive spikes but makes his use of this terminology admirably clear by his statement that "when recordings are made from a distant, relatively inactive reference electrode to the center of the discharging area, the spike discharges are negative to the reference electrode." Stephenson¹⁵⁰ has also found this type of activity in 32 out of 2500 adult patients (but he omits the clarifying statement). Both authors suspect a correlation with epileptic disorder located in the thalamus or hypothalamus, for a reference electrode consisting of the two

ears linked is negative to the scalp electrodes during the spiking, from which they conclude that the superficial layers of the cortex are not involved in the discharge.

The clinical application of activation methods has now been tested in many centers and assessments of the various technics have been made by several independent workers. Taking first the criterion that the chosen method of activation is required to evoke EEG abnormalities in epileptics whose resting records are normal, the various reports are as follows: With photic stimulation alone, Hill⁷⁵ finds less than 5 per cent showing this change, Hutchinson,⁸² 0 per cent (in 100 cases), Walter,¹⁶⁴ 0 per cent (in 2000 cases). However, Rémy¹³⁶ reports three cases and Lloyd-Smith 13.¹⁶⁶ Compared with these figures, seconal sleep was found successful by this criterion in 0 per cent of 60 cases by Hutchinson⁸² and in 13 per cent of 76 cases by Merlis.¹¹⁶ Metrazol alone, by slow injection of divided doses, was found specific in 12 per cent of 100 cases by Hutchinson and in 47 per cent of 58 cases by Merlis. Both workers consequently recommend this as the preferred technic.

A more important criterion, perhaps, is that the method of activation should evoke abnormalities of a nature specific to epilepsy where the resting record, although abnormal, is non-specific.⁶¹ By this criterion, Walter¹⁶⁴ finds photic stimulation alone successful in 32 per cent (37 cases); this figure may be raised by using flashes from multiple sources (Hodge⁷⁸).

A report is now available (Badier¹⁰) on the postmortem findings on five patients in whom myoclonic responses could be evoked by recruitment (without metrazol). The findings were: a cerebellar hemangioma, an ependyoma of the fourth ventricle, an epidermoid cyst of the brainstem and two acoustic neuromas. The authors postulate the common factor to be pressure on, and consequent irritation of, the reticular substance of the brainstem resulting in an irradiated response to the thalamus and cortex.

Reports that activation technics bring out abnormalities similar to epileptic discharges in patients whose clinical diagnosis has been hysteria continue to come in.^{21, 75, 82, 164}

A report from the Laboratoire de Neuroélectrologie at Lyon²¹ gives a useful analysis of the results of activation by photic stimulation combined with metrazol in 400 patients classified in six clinical categories. These workers, Bonnet, Bonnet and Courjon, confirm the original observations made by Rémond and Gastaut in 1949. They agree that although a "positive" activation test is not specific to a clinical category, a "negative" one effectively rules out generalized epilepsy of subcortical origin. The value of the positive result lies, not in the fact that it is positive, but in the information it gives as to the location of the trouble.

There would appear to be a continuum of sensitivity to photic stimulation

ranging from those who require no metrazol for the eliciting of a myoclonic response to those at the other extreme who are very resistant and require a great deal. Where the so-called normal lies in this continuum has been the subject of some debate¹⁷ and was the subject of Kershman's^{91, 92} current researches at the time of his tragic death. It was beginning to emerge that certain differences in technic were the basis for conflicting reports. Schwab¹⁴³ has drawn attention to such variables as intensity of the light source, rate of injection, and anxiety on the part of the patient (resulting in over-breathing). All of this has been discussed in detail by Gastaut,⁶⁴ who considers the first two the most influential and advocates an exact standardization of technics before comparison of thresholds is made. From direct observations of responses (to flash) in the optic nerve, lateral geniculate and visual cortex of the cat, the reviewer has been led to wonder whether another variable may be responsible for reported differences between laboratories, namely, the effect of ambient light in the eye. All responses to a flash of given intensity are increased in amplitude when the room is darkened. (This effect is probably more marked in a predominantly scotopic eye.) Most of the clinical electroencephalographers reporting on this subject have not stated whether their patients were tested with the room light on or off (and if on, whether constant in intensity). The energy distribution in time (e.g., sine wave, square wave, sectorized light, gas tube, etc.) as delivered to the retinal elements would also have an effect on the impulse dispersion in the visual pathways. Some results of Daly's⁴⁰ might suggest this. The wave-length content of the light stimulus is also not the same in all laboratories, a red light being favored in some centers.

That wave-and-spike discharges resembling those encountered in epileptics can be evoked in non-epileptic subjects by a careful timing of paired flashes of light (during metrazol injection) has now been demonstrated by Gastaut.^{64, 137} Although he has found some impairment of consciousness in these artificially induced attacks he has not as yet found true "absences." Cornil³⁵ has published an ingenious modification of Schwab's reaction-time method for testing impairment of consciousness in petit mal. It consists of a circuit by which the wave-spike from the brain triggers the stimulus to which the patient has been instructed to respond. The critical timing, according to Gastaut, is not the rate at which the pairs are repeated, but the interval between the members of the pair, i. e., the second flash of each pair should fall in the supernormal period following the neuronal discharge set up by the first.⁶² Curves of cortical excitability cycles for man^{59, 63} have been published and also for the anesthetized and non-anesthetized cat.¹¹⁹ In a system containing so many elements (including those of the retina), one might expect these curves to represent some form of integrated effect, and that different components would be respon-

sible for various of the factors influencing them in different degrees (e.g., retinal elements reacting primarily to intensity, synapses to barbiturates, etc.). Excitability curves for the auditory cortex have been worked out by Chang³⁰ in animals under barbiturate anesthesia.

An interesting study of wave-spike foci, suggestive of a subcortical origin, yet appearing first and more markedly in one hemisphere has been made by Dell.⁴⁶ Of the nine cases reported, seven had giratory fits. A direct attempt to get evidence on the origin of spike-and-wave activity in human subjects has been made by Spiegel¹⁴⁶ and Wycis. Recordings from the diencephalon have demonstrated the presence of spikes and of spike-and-dome discharges in cases with petit mal attacks but no circumscribed focus was found common to all cases. This work led to the placing of small lesions in the diencephalon in an attempt to relieve seizures in six cases in whom all other therapy had failed. The authors show wisdom in the caution with which they discuss their somewhat equivocal results.

Electroencephalographers concerned with the interpretation of recordings from depth of electrodes are recommended to read Jung's paper on the use of such electrodes inserted through burr holes.⁸⁸ His recordings are exceptionally clear. A design for implanted electrodes for recording and stimulating in the thalamus of cats has been described by Koella and Hess.⁹⁶

Further material from studies with basal leads has been published⁸ and another type of nasal lead has been described.⁷⁰ EEG's recorded with basal leads have also been published from Russia,¹²² arguing the advantage of linkages between these leads and scalp electrodes when searching for deep-lying tumors.

Among the studies of psychomotor epilepsy, Cossa³⁷ brings evidence that psychomotor automatisms are not a disease entity but a sequel to many types of epileptic fits. He finds the psychomotor symptoms developing not during the period of the seizure discharge but during the phase of slow waves and lowered amplitude which follows it, i.e., the impairment of conscious behavior occurs during the period of depressed neuronal activity. He gives excellent illustrations of the EEG in cases of automatism following temporal lobe seizure, petit mal attack and grand mal convulsion.

A discussion of this problem has also been published by Dongier.⁴⁹ Gibbs⁶⁶ in a series of 163 cases with EEG foci in the anterior temporal lobe found 95 per cent had clinical psychomotor seizures. Iobst and Forster⁸⁴ have also published details on a series of 50 patients with temporal lobe dysrhythmia.

The early confidence in the value of focal EEG spiking as an indicator of cortical epileptogenic tissue in other parts of the brain has been questioned in the light of new experience and the knowledge that the focal spike may

have been propagated from a distance. The influence of this on the surgeon's evaluation of EEG spiking in making the decision for or against cortical excision¹ for the treatment of epilepsy has been discussed by Walker.¹⁶³ Bailey and Gibbs,¹¹ however, think that in the cases of psychomotor epilepsy the seizure discharge is primarily temporal in origin and not conducted from deeper areas. Their description of temporal lobe surgery for psychomotor epilepsy reveals great reliance on the EEG findings especially in sleep and during pentothal anesthesia, both of which states were found to activate anterior temporal foci.

Green, who attaches considerable importance to the electrocorticogram,⁷¹ has reported⁷² on the effects of anterior temporal lobectomies in patients with psychomotor epilepsy who failed to respond to medical therapy. In all of his 23 cases focal EEG abnormalities were present in the anterior temporal lobe, and gross or microscopic pathology was found in association with them in 14 of the 23 patients. This paper contains an interesting analysis of the seizure patterns and of the results of surgical treatment, and promises a follow-up report on these patients after some years have passed.

Hoefler and his colleagues⁷⁹ have added to their series (published ten years ago) of cases with paroxysmal abdominal pain as an apparent epileptic equivalent. They now have 31 of these interesting cases, and in 30 per cent of these, the interseizure EEG was abnormal (in four of them it was actually spike-and-wave). However, only 11 were helped by anti-convulsant therapy.

A review of the experience gained in a general hospital from 500 records has been summarized by Arieff⁹ but, as in so many previous reports, the seizure patterns of petit mal have been included with the interseizure patterns of other types of fits to reach a figure of 80 per cent abnormal EEG records in epilepsy. It would be interesting to have data from more centers on the percentage of abnormal interseizure records in all types of epilepsy including petit mal. Presumably the seizure record not only for petit mal but for all types is abnormal. (The purpose of activation is to approximate this record.) Kershman's⁹³ large series of 2648 epileptic patients has demonstrated that focal disturbances are by far the commonest single type of EEG abnormality in epilepsy.

A monograph of work on EEG has been dedicated this year to Professor Bremer. This includes a review of the diagnostic scope of the EEG in epilepsy by Noel.¹²¹ He finds the Gibbs classification more useful than the Montreal classification. Titeca¹⁶⁷ discusses the use of the EEG in assessing medication in epilepsy. A review¹⁶⁹ of clinical electroencephalography that is concisely and explicitly written is, however, disappointing in that, with few exceptions, its statements reflect the state of our knowledge in 1941

rather than in 1951. The illustrations are a challenge to our detective abilities since the derivations are not indicated.

In the search for early electrical signs of tumor growth some progress has been made. In gliomas, where early diagnosis is of prime importance, Chavany³² finds EEG signs occurring before x-ray signs or changes in the eyegrounds.

Disturbed by some of the reports of untoward effects resulting from the use of contrast media for cerebral angiography, Bloor^{19, 20} has used simultaneous EEG recordings as a measure for subtle changes in cerebral physiology occurring during injection of the dye and has correlated these changes with postmortem histologic findings in rabbits and monkeys. Diodrast was found to be the least noxious of several media examined.

In thrombosis of the major cerebral arteries Jones and Bagchi³⁶ find that the EEG more frequently lateralizes than locates the site of damage. Serial EEGs, however, usually bring out a differentiation between thrombosis and neoplasm. From a large series of aneurysms, Roseman¹³⁹ concludes that the EEG definitely aids in lateralizing and may indicate location of the lesion. In experimental occlusion of the middle cerebral artery in animals, however, Harvey⁷³ finds that the resultant abnormalities are not necessarily restricted to the side of the lesion.

Some of the EEG clues to the presence of a subdural hematoma have now been formulated empirically from surgically verified cases. The experiences of Sullivan¹⁵³ (32 cases), Friedlander⁵⁶ (39 cases) and Marinacci¹¹³ (7 infants) will all prove useful guides to the clinical electroencephalographer. Martin¹¹⁴ describes some interesting observations made during sleep on a case of one-sided hematoma. The EEG both during wakefulness and sleep was profoundly asymmetrical but the evoked response to a noise during sleep appeared in both hemispheres. The clinical significance of hemispheric asymmetry in EEG tracings has been examined in some detail by Aird⁴ who finds it of considerable value in locating lesions.

In an analysis of 50 cases of closed head injury, Courjon³⁸ finds the EEG of great prognostic help. In those cases where the EEG was normal (even with photic stimulation) all recovered from their neurologic defects without surgical intervention. Serial EEG's ameliorating progressively with the clinical signs are also contraindicative of surgery. Local abnormalities persisting in spite of clearing clinical symptoms are thought to presage trouble, usually the eventual development of epilepsy. In eight operated cases with previously localized EEG signs, three had hematomas and one cerebral softening. Where diffuse EEG abnormalities are found the author advises against surgical intervention. Another series has been published by Clark and Harper³³ who contrast the EEG findings with those in "open" head injuries.

In patients with a history of head injury, but with no clinical signs, Weil¹⁶⁸ found 41 per cent to have EEG irregularities indicative of cerebral pathology. Much has been claimed for the value of serial EEG's in such cases and now some data have become available on 45 cases. R. Dawson⁴² finds the EEG changes to lag behind the clinical changes (in either direction, i.e., recovery or deterioration). General suppression of activity when it occurred early (i.e., within 30 hours of the injury) was invariably fatal. The authors interpret their findings of focal and general suppressions as in agreement with those of Leão in rabbits. Mechanical stimulation of the cortex in these animals produces depression and even extinction of activity in the area stimulated. With strong stimulation the suppression may spread and become complete over the entire brain. Leão⁷⁸ has published some new work from which he concludes that the early stages of voltage variation of spreading depression are identical with those produced by circulatory arrest, and in which he traces the potential changes in succeeding layers of the cortex. Marshall¹¹¹ has discussed the criticisms of Van Harreveld¹⁶⁰ who has presented some data on the reversible effects of exposure of the cat's cortex to high concentrations of potassium, a condition conducive to spreading depression, as is also cooling of the cortex,¹¹⁰ and exposure to air.¹⁰⁹

More information is now available about the "diffuse" thalamic projection system on the one hand and the reticular activating system on the other. In the case of the first, the thalamic stations are found by Starzl and Magoun¹⁴⁷ to be, in the cat, the center median and intralaminar nuclei (confirming Dempsey and Morison), the ventralis anterior and anterior nuclei, and the cephalic pole only of the thalamic reticular nucleus (not the whole nucleus as proposed by Jasper and by Rose and Woolsey). They find these nuclei so closely interconnected at the thalamic level that stimulation (of the strength used in these experiments) of any one of them excites the others, thus producing a mass discharge with resultant effect at the association areas of the cortex; the receiving areas for this diffuse thalamic discharge are not themselves diffuse but are as clearly delimited in cortical zones as are the specific primary receiving areas, into which, according to these workers they do not trespass. Marsan and Jasper⁵ have, however, reported some projection of these systems into the primary visual cortex. Nor can Starzl and Magoun¹⁴⁷ find any electrophysiologic evidence (using the recruiting response as their criterion) that the intralaminar nuclei project to relays in the cortex of the rhinencephalon, or that the reticular nucleus in its entirety plays the main role as relay station for a diffuse projection system.

Some workers will be worried that ablation of the neocortex is not followed by degenerative changes in the cells of these thalamic nuclei.

Starzl and Magoun, however, are satisfied that collaterals of these thalamo-cortical afferents could be sufficient to keep the cell bodies viable.

From their studies of the reticular activating system in the brainstem, Starzl, Taylor and Magoun¹⁴⁸ conclude that the diffuse thalamic projection system plays only a minor role in the ascending pathways. They located the main thalamic relay in the ventromedial part of the thalamus but an extrathalamic path from the sub- and hypothalamus into the internal capsule was also found. This was the route originally suggested by Forbes for the "secondary" cortical response. The secondary cortical response of Forbes, and of Dempsey and Morison is invoked by Dell¹⁴⁵ to explain the evolution of the slow wave component of the cortical epileptic discharges produced in the cat by sensory stimulation during injection of metrazol.

That the brainstem reticular system receives collaterals from the ascending specific somatic and auditory afferents seems indubitable,¹⁴⁹ the evidence from earlier degeneration studies now being supported by electrophysiologic data. The experimental fact that arousal follows stimulation of the brainstem reticular system is now clearly reconciled with the everyday observation that afferent stimuli can wake the sleeper. Strong alerting stimuli can even break through the "sleep" of animals whose hypothalamus has been destroyed as has been shown by a detailed study by Ingram⁸³ of the role of the hypothalamus in the cortical activity of chronically prepared animals.

Arduini and Terzuolo⁷ have studied the polarity of the recruiting response by investigating the effects of asphyxia, local cocainization, and removal of cortical gray matter. The positive recruited potentials survive cortical ablation and hence seem identical with what Adrian called "afferent cortical waves;" hence, recruitment would appear to have taken place not on the cortex but in the thalamus. The surface negative responses of the cortical neurones can also be differentially extinguished by asphyxia or cocaine. The waxing and waning of the recruiting response, judged by the same criteria, also appears to be thalamic.

Thus, evidence is collecting that diffuse activation of the cortex may not require the concept of non-specific thalamo-cortical fibers but may be rendered diffuse by intrathalamic connection and carried to the cortex by the known specific projection pathways. Systematic serial ablation of thalamic nuclei may be one way of gaining evidence on this controversial issue although it is difficult to design the critical experiment. Work along these lines is now in progress in the Montreal laboratories (Jasper⁸⁵).

In attempting to interpret all the recent work from the various laboratories on the diffuse activation of the cortex, McLardy's¹¹⁸ clarifying critique is most valuable. In this paper, he assembles the evidence for the observed diffusion being intrathalamic in location, the pathways to the cortex being

the recognized specific afferents from the thalamic specific projection nuclei. Degeneration studies militate against the existence of direct projections to the neocortex from the intralaminar nuclei (nuclei centralis lateralis, paracentralis, centralis medialis and centromedian) but there is evidence of projection from the intralaminar nuclei to the caudate nucleus and from the centromedian to the putamen (Fortuyn⁵⁵). Nor do degeneration studies give any stronger support to a cortical projection from the reticular nucleus. McLardy suggests that Jasper's finding that cortical recruitment can be evoked by electrical stimulation of the medial intralaminar nuclei may be interpreted as an activation of fibers passing close to the centromedian nucleus and coming from cell bodies in or near the anterior or cingulate region. Fortuyn⁵⁵ makes a somewhat similar suggestion. One wonders whether possibly the differential effect of drugs (perhaps acetylcholine) might be used to examine this point or the differential destructive action of ultrasound on cells rather than fibers (Wall^{163a}). Such an interpretation would explain the failure to elicit recruitment by introduction of strychnine into the massa intermedia as demonstrated by Cohn in 1949.

In the search for new anticonvulsants, several drugs have been tested for their effects on the abnormal EEG's of epileptics. Water-soluble desoxycorticosterone gluconide (I.V.) produces a small but consistent decrease in the frequency of abnormal waves in patients unresponsive to other forms of therapy (Aird³). Glutamic acid (Pond¹³¹) also seems to decrease the amount of spike-and-wave activity in patients with petit mal, but the effect is slight and only transitory. The use of this drug and of many other anticonvulsants has been reviewed this year by Aird.² The effects on the EEG of prolonged treatment by ACTH and of cortisone are only slight.^{57, 130, 159}

In a study of the effect of different anesthetics on the electrocorticograms of patients at operation, Woring¹⁷⁰ concludes that nitrous oxide is the least likely to mask epileptic activity (ether masks it almost completely). Concurrent studies in animals suggest different mechanisms for the actions of various anesthetics and not a simple effect produced by inhibition of the cerebral metabolism.¹⁴¹

EEG correlates for levels of anesthesia have been published for nitrous oxide and ether (Courtin³⁹) and for pentothal (Kiersey⁹⁴). The EEG patterns of the latter are in close agreement with those published by Brazier.²³ The results vary in many respects from those published last year by Schneider for nitrous oxide. Bickford's^{15, 16} development of his servo-mechanism for automatic control of anesthesia employs selection and integration of certain frequencies by the circuits of an automatic frequency analyzer so that artifacts and interference outside this range have no part in the feed-back system. Verzeano¹⁶¹ has published a modification eliminat-

ing the use of tubes and relays. Swank¹⁵⁴ has found that barbiturates produce the same effect on the fast cerebellar potentials (1000–2000 c/s) as they do on the cerebral activity.

Faure⁵² has continued his search for changes in the EEG evoked by emotional stress and intellectual effort. The present report is restricted to the behavior of the alpha rhythm, whereas possibly a study of the rhythms from the anterior temporal lobes (not linked to the occiput) might have proved more fruitful. He concludes that alpha instead of being a rhythm of repose, is, in fact, a release phenomenon appearing on relief from pain, on achievement of a solution and on release from tension. He has incorporated the EEG in a battery of recordings made during psychiatric interviews⁵² under narcoanalysis and has used a Walter analyzer in correlating his results with simultaneous changes in skin resistance, respiration, electromyograms, and microphone recordings of the interview.

Hill's⁷⁷ investigations of the disturbance of homeostatic mechanisms in schizophrenic patients exposed to stress (insulin hypoglycemia) also employ simultaneous recordings of the EEG, palmar skin resistance and heart rate. Use has been made of the several types of information made available by automatic frequency analysis—especially in the detection and quantification of 6 c/s activity appearing as a new rhythm at a stage in the hypoglycemic response. This theta activity appears sooner (i.e., at a higher level of blood sugar) in normal subjects than in schizophrenics. Some normal standards for the occurrence of theta (and beta) activity have been published by Mundy-Castle¹²⁰ for healthy adults in two widely disparate age groups. We still have more hypotheses about the theta rhythms than we have data.

A line of investigation which is new (although it owes its basic suggestion to Cushing) is the study of the effects on the activity of the brainstem reticular area in cats of intraventricular injection of acetylcholine on the one hand, and of cholinesterases on the other. The outcome of these experiments led to the interruption of long-persisting stupor in four catatonic schizophrenics by intraventricular cholinesterase. There was a concomitant change in the insulin tolerance curve and in alpha production in the direction of the norm (Sherwood¹⁴⁴).

Two studies have appeared on the effect on the EEG of lowering the body temperature in animals that hibernate. Kayser⁹⁰ finds activity still present at 10° C in gophers, but absent at 5° C, at which temperature the heartrate is reduced to 10 beats per minute. In hamsters, although the body temperature may drop to 2.5° C during hibernation, no EEG reappears until the temperature rises to 19° C (Chatfield³¹). In these conditions electrical silence of the brain, although immensely prolonged, is clearly a reversible process.

In the field of apparatus development, the toposcope of Walter and Shipton^{166, 167} has now been published in considerable detail and with a block diagram of the circuit. This ingenious method will probably prove to be more readily applicable to study of EEG responses to rhythmic sensory stimulation than to some other types of activity, for there is some frequency selection imposed by the rotational speed chosen for the radius vector (although this can be controlled). Knott⁹⁵ has published construction notes on the automatic frequency analyzer he has built after the Walter design using readily available American components, and Krakau⁹⁷ has described an optical method of analysis based on density modulation of a photographic film. Drohocki⁵⁰ has discussed some of the limitations of the various types of analyzers now in use and presents a schema for a spectrograph designed to overcome some of the errors introduced by the use of resonating circuits. It employs a system of modulation, the EEG potentials causing amplitude modulation of the output of a variable oscillator. This oscillator periodically covers a range from 800 to 860 c/s so that superimposed EEG frequencies of from 1 to 60 are consecutively selected by a single filter and recorded as vertical deflections of a cathode ray trace. Here they are identifiable as to frequency by their position along the abscissa formed by the horizontal sweep (this being triggered by the regulator of the oscillator's frequency). The use of a single, widely selective filter, overcoming the difficulty introduced by the long time-constants of more highly selective circuits, is the major advantage claimed by the designer.

The pros and cons, design and maintenance, application and fruitfulness of automatic analysis were the subjects for discussion at a meeting convened for this purpose in June of this year.³⁴ This was attended by representatives from ten laboratories in the United States where such methods are now in use. All who are using this technic should read the criticism offered by a mathematician (Vogel) in a discussion with Walter.¹⁶²

It now seems generally agreed that an indifferent electrode does not exist anywhere on the volume conductor we call the human body. It remains for us to choose the least misleading of the available reference leads. In a careful comparative study, Corriol³⁶ analyzes the advantages and disadvantages of four common reference leads: the lobe of the ear, the two ears linked, the non-cephalic reference electrode proposed by Stephenson and Gibbs¹⁵¹ and the average electrode recommended last year by Offner. His conclusions are that the first of these is only adequate for a strictly contralateral focus; the second is virtually useless; the third, being off the head, is indicated when the dysrhythmia is bilateral; the fourth proves to be more satisfactory in practice than in theory, especially if the electrodes nearest to the focus are disconnected from the average. Corriol recommends

finding the focus by bipolar methods and deciding from these findings which reference lead to use for further investigation. This paper is important in that it emphasizes that the choice of reference lead will influence the recording obtained, something a truly indifferent lead would never do. Nietzsche is invoked to warn us that our choice will load the dice. This reviewer has previously proposed, and Corriol concurs, that the plotting of electrical fields in EEG work will serve to sort out activity brought in by the reference lead. Rémond¹³⁴ has plotted the field for eye-blinks, a study which will be valuable to clinical electroencephalographers searching for signs of frontal lobe tumor. Monnier^{117, 118} has also made a detailed study of eye movements (including nystagmus) and has used nasal leads as well as surface electrodes in his exploration.

Thiry¹⁵⁶ recommends recording push-pull with the average electrode leading not only to the reference grid through a high resistance but also to the grid which receives the input from the active lead. In this way, instabilities in the average lead itself being in phase and of the same magnitude on both grids will not be amplified by push-pull circuits and hence will not be recorded. This short report does not contain enough details (as for example, ratio of resistance used to the resistance to ground) for the reader to be able to judge for himself what effect this would have on the value above ground of the exploring electrode. One gains the impression that only an approximation of the desired result could be given by this method and that interference pick-up would be a real hazard.

One might wonder, when such difficulties lie in the way of finding a satisfactory reference lead, why electroencephalographers should still want to record by "unipolar" leads. Apart from the information it brings to the plotting of fields, many workers find a reference lead of practical help in tumor location provided they can be alert to any false clues it may introduce. A study of this question has been made this year by Fischgold⁵⁴ in a series of intracranial tumors. He finds the earlobe almost useless, for in deep lesions it is nearly always active. He finds the nose, the chin and non-cephalic reference of Stephenson and Gibbs¹⁵¹ all useful, though the manipulation of the potentiometer in the last method is too time-consuming with very sick patients and not always satisfactory. In his experience, the average electrode gives the best results, although again it is contraindicated when the EEG abnormalities are generalized.

Among the recently developed electrodes¹²⁸ are a 7 cm. long needle inserted under local anesthesia until the tip rests against the sphenoid wing, and a curved orbital lead inserted until it rests against the roof of the orbit. The latter requires no anesthetic for its introduction and records primarily from the orbital surface of the brain whereas the former (which appears to resemble those described previously by Jones and Kristiansen)

records mainly from the under surface of the temporal lobe. These would appear to be tools for the neurosurgeon rather than for the electroencephalographer. Examples of application of their use will be found in the discussion on the surgical treatment of epilepsy published by the neurosurgical clinic at la Pitié.¹²⁹ This article gives a careful assessment of the authors' experience with cortical excision in the absence of tumors.

The EEG has been used in attempts to find the locus of effect of electric shock treatments⁴³ and as a method for controlling the shock technic and for assessing this form of treatment.¹⁴⁰ In newborn animals (rats) the EEG is not affected by electroshock until the 4th or 5th day, and no convulsion can be induced until the 7th day.¹⁵³ Fortunately, there are no data on the effects in newborn humans.

Of interest to all concerned with medico-legal problems is Hill's and Pond's⁷⁶ report on the EEGs of 105 murderers (an extension of the series published previously by Stafford-Clark and Taylor). Eighteen of these cases were epileptics, but over half had abnormal EEGs. In a smaller series, Delay⁴⁴ also found a high incidence of abnormal EEGs. He also examined prisoners accused of lesser crimes.

An assessment of the use of the EEG in psychiatry has been given by Rémy.¹³⁵ In child psychiatry, the leading contribution has been the paper by Hill⁷⁴ with its wise presentation of the present state of our knowledge. Emphasis is put on delayed maturation as being a likely etiologic factor behind both the behavior disorders and their accompanying EEG abnormalities; the trend towards the study of EEG responses to stress is welcomed as this promises to be more fruitful than study of the resting record.

In other branches of pediatrics the EEG has been found useful in such problems as the detection of brain damage causing hearing loss in very young children (Marcus¹⁰⁸), and in the evaluation of neuro-ocular pathology (Levinson¹⁰⁰). In acute purulent meningitis the EEG may detect damage to the brain which is not obvious on clinical evaluation alone (Hughes⁸⁰) although the opposite may also occasionally happen, viz., a normal EEG in spite of persisting clinical signs. Some results are now available on the EEG signs of tubercular meningitis. Passouant,¹²⁷ from a study of 500 tracings from 150 cases, has been able to establish prognostic criteria based primarily on a differentiation between diencephalic and cortical involvement. In epileptic convulsions in children, Berlin¹³ makes a plea for more recognition of an emotional factor influencing the severity of the symptoms.

In a series of 70 cases of infantile hemiplegia, Bezos and Lérique-Koechlin¹⁴ found the EEG only rarely to be normal and believe it to be useful in weighing the pros and cons of surgical intervention. EEG tracings in single cases of sporadic subacute encephalitis have been described by each of two authors^{133, 155} with characteristics in essential agreement with those de-

scribed a few years ago by Cobb and Hill. The abnormalities they described (marked periodic bursts) differ from those of the commoner encephalitides.

Results from studies⁶⁷⁻⁶⁹ of the correlation between steady cortical potentials and the EEG are impinging more and more on the interpretation of the latter, and users of standard resistance-coupled amplifiers are realizing the restrictions imposed by their apparatus on the information they derive.

A survey of this year's work in electroencephalography shows that it is being used to attack the basic problems of the nervous system from two angles: on the one hand, to observe the total pattern and break it down into its components; on the other, to study the component parts and build them into a whole. A welding of the two approaches promises the most.

REFERENCES

- ¹ Achslogh, J. and Ectors, L.: L'électro-corticographie dans le traitement chirurgical de l'épilepsie focale. *Bull. Soc. Clin. Hôp. Charleroi.* 2:155-176, 1951.
- ² Aird, R. B.: Modern advances in the diagnosis and treatment of convulsive disorders. *Am. Pract. & Digest. Treat.* 2:777-781, 1951.
- ³ — and Gordon, G. S.: Anticonvulsant properties of desoxycorticosterone. *J.A.M.A.* 145:715-719, 1951.
- ⁴ — and Zeale, D. S.: The localizing value of asymmetrical EEG tracings obtained simultaneously by homologous recording. *EEG. Clin. Neurophysiol.* 3:487-495, 1951.
- ⁵ Ajmone-Marsan, A. C. and Jasper, H. H.: A. Research Nerv. & Ment. Dis., Proc. 1950. In press.
- ⁶ Albe-Fessard, D. and Buser, P.: Données sur l'orientation de certaines activités électriques du cortex. *Rev. neurol.* 84:593-595, 1951.
- ⁷ Arduini, A. and Terzuolo, C.: Cortical and subcortical components in the recruiting responses. *EEG Clin. Neurophysiol.* 3:189-196, 1951.
- ⁸ Arellano, A. P. and MacLean, P. D.: Basal electroencephalography: some findings. *J. Nerv. Ment. Dis.* 113:485-496, 1951.
- ⁹ Arieff, A. J.: Electroencephalography in a general hospital—Resumé of 500 records. *Quart. Bull., Northwestern Univ. M. School.* 25:342-344, 1951.
- ¹⁰ Badier, M. and Gastaut, H.: Étude anatomique de cinq malades présentant une réponse myoclonique par recrutement sans l'aide de cardiazol. *Rev. neurol.* 84:676-677, 1951.
- ¹¹ Bailey, P. and Gibbs, F. A.: The surgical treatment of psychomotor epilepsy. *J.A.M.A.* 145:365-370, 1951.
- ¹² Bates, J. A. V.: The electrical activity of the cortex accompanying movement. *J. Physiol.* 111:240-257, 1951.
- ¹³ Berlin, I. N. and Yeager, C. L.: Correlation of epileptic seizures, EEG and emotional state. *Am. J. Dis. Child.* 81:664-670, 1951.
- ¹⁴ Bezos, Mme. and Lérique-Koechlin, A.: Données fournies par l'EEG dans 70 cas d'hémiplégie cérébrale infantile. *Rev. neurol.* 84:687-691, 1951.
- ¹⁵ Bickford, R. G.: The use of feed-back systems for the control of anesthesia. *Elect. Eng.* 70:852-855, 1951.
- ¹⁶ —: Use of frequency discrimination in the automatic electroencephalographic control of anesthesia (servo-anesthesia). *EEG Clin. Neurophysiol.* 3:83-86, 1951.

- ¹⁷ — and Daly, D.: Experiences with the photometrazol test. *Proc. Eastern EEG Assoc. EEG Clin. Neurophysiol.* 3:378, 1951.
- ¹⁸ Bishop, G. H. and Clare, M.: Radiation path from geniculate to optic cortex in cat. *J. Neurophysiol.* 15:497-506, 1951.
- ¹⁹ Bloor, B. M., Wrenn, F. R., and Hayes, C. J.: An experimental method for the evaluation of contrast media used in cerebral angiography. *J. Neurosurg.* 8:435-440, 1951.
- ²⁰ Bloor, B. M., Wrenn, F. R., and Margolis, G.: An experimental evaluation of certain contrast media used for cerebral angiography. *J. Neurosurg.* 8:585-594, 1951.
- ²¹ Bonnet, H., Bonnet, V., and Courjon, J.: Corrélations électrocliniques dans 400 cas activation photocardiazolique. *Rev. neurol.* 84:614-619, 1951.
- ²² Boudin, G., Rémond, A., and Castaigne, P.: Étude électroencéphalographique d'une hypoglycémie spontanée par adénome des îlots de Langerhans. Considérations sur les modifications électroencéphalographiques de hypoglycémie. *Rev. neurol.* 84:171-174, 1951.
- ²³ Brazier, M. A. B.: *The Electrical Activity of the Nervous System*. London, Sir Isaac Pitman & Sons Ltd.: New York, Macmillan, 1951, 220 pp.
- ²⁴ — and Casby, J. U.: An application of the M. I. T. digital electronic correlator to a problem in EEG: The EEG during mental calculation. *Proc. Eastern Assoc. EEG Clin. Neurophysiol.* 3:375, 1951.
- ²⁵ — and Casby, J. U.: A study of the EEG in normal subjects during intermittent photic stimulation. *Proc. Am. EEG Soc. EEG Clin. Neurophysiol.* In press.
- ²⁶ Bremer, F. and Bonnet, V.: Caractères généraux de la réponse du cervelet à une volée d'influx afférents. *Congrès des Physiologistes de langue française*. Liège, 1951.
- ^{26a} —: Convergence et interaction des influx afférents dans l'écorce cérébelleuse, principe, fonctionnel du cervelet. *Congrès des Physiologistes*, Liège, 1951.
- ²⁷ Burns, B. D.: Some properties of isolated cerebral cortex in the unanaesthetized cat. *J. Physiol.* 112:156-175, 1951.
- ²⁸ Jeffress, L. A., Brosin, H. W., Halstead, W. C., Klüver, H., Köhler, W., Lashley, K. S., McCulloch, W. S., and von Neumann, J.: *Cerebral mechanisms in behavior*. Hixon Symposium. New York, Wiley, 1951, p. 311.
- ²⁹ Chang, H. T.: Dendritic potential of cortical neurons produced by direct electrical stimulation of the cerebral cortex. *J. Neurophysiol.* 14:1-21, 1951.
- ³⁰ —: Changes in excitability of cerebral cortex following single electric shock applied to cortical surface. *J. Neurophysiol.* 14:95-112, 1951.
- ³¹ Chatfield, P. O., Lyman, C. P., and Purpura, D. P.: The effects of temperature on the spontaneous and induced electrical activity in the cerebral cortex of the golden hamster. *EEG Clin. Neurophysiol.* 3:225-230, 1951.
- ³² Chavany, J. A., Arfel-Capdeville, G., Guiot, G., and Fischgold, H.: L'EEG dans de diagnostic des gliomes; incidences thérapeutiques, *Rev. neurol.* 84:459-466, 1951.
- ³³ Clark, E. C. and Harper, E. O.: Electroencephalographic findings in 186 cases of chronic post-traumatic encephalopathy. *EEG. Clin. Neurophysiol.* 3:9-14, 1951.
- ³⁴ Conference: Analyzers and the theory of analysis. (Abstract). *EEG Clin. Neurophysiol.* 3:385, 1951.
- ³⁵ Cornil, L., Gastaut, H., and Corriol, J.: Appréciation du degré de conscience au cours des paroxysmes épileptiques "Petit Mal." *Rev. neurol.* 84:149-151, 1951.

- ³⁶ Corriol, J. H.: Méthodes EEG d'enregistrement unipolaire et bipolaire. *Rev. neurol.* 84:554-569, 1951.
- ³⁷ Cossa, P. and Martin, P.: L'automatisme psychomoteur des épilepsies. *Rev. neurol.* 84:317-327, 1951.
- ³⁸ Courjon, J. and Bonnet, H.: Les renseignements fournis par l'EEG dans la surveillance des traumatismes fermés du crâne durant les trois premières semaines. *Rev. neurol.* 84:669-671, 1951.
- ³⁹ Courtin, R. F.: The value of continuous EEG and electrocardiographic tracings to the anesthetist during surgery. *Brit. J. Anaesth.* 23:5-13, 1951.
- ⁴⁰ Daly, D. and Bickford, R. G.: Electroencephalographic studies of identical twins with photo-epilepsy. *EEG Clin. Neurophysiol.* 3:245-249, 1951.
- ⁴¹ Dawson, G. D.: A summation technique for detecting small signals in a large irregular background. *Proc. Physiol. Soc. J. Physiol.* 115: 1951.
- ⁴² Dawson, R. E., Webster, J. E., and Gurdjian, E. S.: Serial electroencephalography in acute head injuries. *J. Neurosurg.* 8:613-630, 1951.
- ⁴³ Delay, J., Djournio, A., and Verdeaux, G.: Les nouvelles techniques de l'électrochoc. *Encéphale.* 5:426-483, 1951.
- ⁴⁴ —, Bachet, M., Verdeaux, G., and Verdeaux, J.: L'électroencéphalographie chez les délinquants adultes. *Annales medico-psychologiques.* In press.
- ⁴⁵ Dell, M. B., Bonvallet, M., and Dell, P.: Evolution corticale des crises épileptiques provoquées chez le chat. *Rev. neurol.* 84:595-602, 1951.
- ⁴⁶ — and Hecaen, H.: Complexes pointe-ondes à début unilatéral et épilepsie giratoire. *Rev. neurol.* 84:657-659, 1951.
- ⁴⁷ Dell, P. and Olson, R.: Projections thalamiques corticales et cérébelleuses des afférences viscérales vagues. *Compt. rend. Soc. de biol.* 114:1084-1088, 1951.
- ⁴⁸ —: Projections "secondaires" mésencéphaliques, diencéphaliques et amygdaliennes des afférences viscérales vagues. *Comp. rend. Soc. de biol.* 114:1088-1091, 1951.
- ⁴⁹ Dongier, M. and Gastaut, H.: Sur les troubles psychiques de l'épilepsie dite temporale. *Bull. Hôp. civil de Charleroi.* 2:178-184, 1951.
- ⁵⁰ Drohocki, Z.: Électrospectrographe panoramique du cerveau. *Rev. neurol.* 84:629-632, 1951.
- ⁵¹ Eccles, J. C.: Interpretation of action potentials evoked in the cerebral cortex. *EEG Clin. Neurophysiol.* 3:449, 464, 1951.
- ⁵² Faure, J.: Contribution à l'étude dynamique rythme alpha. *Rev. neurol.* 84:691-697, 1951.
- ⁵³ —, Crenes, R., Dutertre, F., and Lafon, R.: Étude électroencéphalographique de trente-deux narco-analyses. *Rev. neurol.* 84:697-703, 1951.
- ⁵⁴ Fischgold, H. and Dell, M. B.: Utilité des montages dit 'monopolaires' dans la localization de tumeurs intracrâniens. *Rev. neurol.* 84:588-592, 1951.
- ⁵⁵ Fortuyn, J., Droogleever and Stefens, R.: On the anatomical relations of the intralaminar and midline cells of the thalamus. *EEG Clin. Neurophysiol.* 3:393-400, 1951.
- ⁵⁶ Friedlander, W. J.: The electroencephalographic findings in 39 surgically proven subdural hematoma. *EEG Clin. Neurophysiol.* 3:59-62, 1951.
- ⁵⁷ — and Rottger, E.: The effect of cortisone on the electroencephalogram. *EEG Clin. Neurophysiol.* 3:311-313, 1951.
- ⁵⁸ Gastaut, H.: The electrical activity of the brain. *Ann. Rev. Physiol.* 13:297-326, 1951.
- ⁵⁹ —, Gastaut, Y., Roger, A., Corriol, J., and Naquet, R.: Étude électrographique du cycle d'excitabilité cortical. *EEG Clin. Neurophysiol.* 3:401-428, 1951.

- ⁶⁰ —: Manifestations électrographiques de l'activité des voies optiques. *Riv. neurol.* 21:1-27, 1951.
- ⁶¹ —: L'épilepsie photogénique. *Rev. praticien.* 1:1-5, 1951.
- ⁶² — et Corriol, J.: Note préliminaire sur un procédé nouveau et particulièrement efficace de stimulation lumineuse intermittente. *EEG Clin. Neurophysiol.* 3:87-88, 1951.
- ⁶³ —, Corriol, J., and Roger, A.: Le cycle d'excitabilité des systèmes afférents corticaux chez l'homme. *Rev. neurol.* 84:602-605, 1951.
- ⁶⁴ — and Roger A.: Les formes expérimentales de l'épilepsie. III provocation chez l'homme non épileptique des éléments cliniques et électrographiques du Petit Mal: myoclonies et absences, polypointes et pointesondes. *Rev. neurol.* 84:94-99, 1951.
- ⁶⁵ Gibbs, E. L. and Gibbs, F. A.: EEG evidence of thalamic and hypothalamic epilepsy. *Neurology* 1:136-144, 1951.
- ⁶⁶ Gibbs, F. A.: Ictal and non-ictal psychiatric disorders in temporal lobe epilepsy. *J. Nerv. & Ment. Dis.* 113:522-528, 1951.
- ⁶⁷ Goldensohn, E. S., Schoenfeld, R. L., and Hoefer, P. F. A.: The slowly changing voltage of the brain and the electrocorticogram. *EEG Clin. Neurophysiol.* 3:231-236, 1951.
- ⁶⁸ Goldring, S. and O'Leary, J. L.: Experimentally derived correlates between ECG and steady cortical potential. *J. Neurophysiol.* 14:275-288, 1951.
- ⁶⁹ —: Summation of certain enduring sequelae of cortical activation in the rabbit. *EEG Clin. Neurophysiol.* 3:329-340, 1951.
- ⁷⁰ Gottschalk, L. A.: A nasopharyngeal lead of new design. *EEG Clin. Neurophysiol.* 3:511-512, 1951.
- ⁷¹ Green, J. R., Dunsberg, R. E. H., and McGrath, W. B.: Electrocorticography in psychomotor epilepsy. *EEG Clin. Neurophysiol.* 3:293-299, 1951.
- ⁷² —: Focal epilepsy of psychomotor type. A preliminary report on observations on effects of surgical therapy. *J. Neurosurg.* 8:157-172, 1951.
- ⁷³ Harvey, J., and Rasmussen, T.: Electroencephalographic changes associated with experimental temporary focal cerebral anemia. *EEG Clin. Neurophysiol.* 3:341-351, 1951.
- ⁷⁴ Hill, D.: Électroencéphalographie en psychiatrie de l'enfant. Centre International de l'enfance: Travaux et Documents II. Paris, 1951.
- ⁷⁵ —: Discussion on recent advances in the EEG diagnosis of epilepsy. *Proc. Roy. Soc. Med.* 44:332, 1951.
- ⁷⁶ — and Pond, D. A.: Reflections on 100 capital cases submitted to electroencephalography. *J. Ment. Sc.* In press.
- ⁷⁷ —, St. Loe, P., Theobald, J., and Waddell, M.: A central homeostatic mechanism in schizophrenia. *J. Ment. Sc.* 97:111-131, 1951.
- ⁷⁸ Hodge, R. S.: Photic stimulation by multiflash as a diagnostic measure in cerebral dysrhythmia. *Proc. Roy. Soc. Med.* 44:321-322, 1951.
- ⁷⁹ Hoefer, P. F. A., Cohen, S. M., and Greeley, D. M.: Paroxysmal abdominal pain a form of epilepsy in children. *J.A.M.A.* 147:1-6, 1951.
- ⁸⁰ Hughes, J. G., Davis, B. C., and Carpenter, A. E.: Relationship of EEG findings to clinical factors during and after purulent meningitis. *Am. J. Dis. Child.* 82:268-281, 1951.
- ⁸¹ Hunt, W. E. and Goldring, S.: Maturation of evoked response of the visual cortex in the post-natal rabbit. *EEG Clin. Neurophysiol.* 3:465-471, 1951.
- ⁸² Hutchinson, J. T.: Discussion on recent advances in the EEG diagnosis of epilepsy. *Proc. Roy. Soc. Med.* 44:325-331, 1951.

- ⁸³ Ingram, W. R., Knott, J. R., Wheatley, M. D., and Summers, T. D.: Physiological relationships between hypothalamus and cerebral cortex. *EEG Clin. Neurophysiol.* 3:37-58, 1951.
- ⁸⁴ Iobst, C. W. and Forster, F. M.: EEG foci in temporal lobes. *Neurology.* 1:309-317, 1951.
- ⁸⁵ Jasper, H. H.: Personal communication.
- ⁸⁶ Jones, E. V. and Bagchi, B. K.: Electroencephalographic findings in verified thrombosis of major cerebral arteries (14 cases). *Univ. Michigan Bull.* 17:295-310, 1951.
- ⁸⁷ Jung, R.: *Électrophysiologie de la crise convulsive chez l'animal et chez l'homme.* Geneva Symposium, 1951.
- ⁸⁸ —, Riechert, T. and Meyer-Mickeleit, R. W.: Über intracerebrale Hirnpotentialableitungen bei hirnchirurgischen Eingriffen. *Deutsche Ztschr. Nervenhe.* 162:52-60, 1950.
- ⁸⁹ Kaada, B. R.: Somato-motor, autonomic and electrocorticographic responses to electrical stimulation of rhinencephalic and other structures in primates, cat and dog. *Acta. physiol. Scandinav.* 23: Suppl. 83, 285 pp., 1951.
- ⁹⁰ Kayser, C., Rohmer, F., and Hiebel, G.: L'EEG de l'hibernant, léthargie et réveil spontané du spermophile. Essai de reproduction de l'EEG chez le spermophile réveillé et le rat blanc. *Rev. neurol.* 84:570-578, 1951.
- ⁹¹ Kershman, J.: Photic-metrazol activation in normal subjects and in various clinical conditions. *Proc. Am. EEG Soc. EEG Clin. Neurophysiol.* 3:383, 1951.
- ⁹² —: Combined photic-metrazol activation in normal subjects and in psychoneurotic and schizophrenic patients. *Proc. Eastern EEG Assoc. EEG Clin. Neurophysiol.* 3:377-378, 1951.
- ⁹³ —, Vasquez, J., and Goldstein, S.: The incidence of focal and non-focal EEG abnormalities in clinical epilepsy. *EEG Clin. Neurophysiol.* 3:15-24, 1951.
- ⁹⁴ Kiersey, D. K., Bickford, R. G., and Faulconer, A.: EEG patterns produced by thiopental sodium during surgical operations. *Brit. J. Anaesth.* 23:141-152, 1951.
- ⁹⁵ Knott, J. R., Woollery, A., and Randall, J.: Construction notes on an American equivalent of the Walter analyzer. *EEG Clin. Neurophysiol.* 3:91-96, 1951.
- ⁹⁶ Koella, W., Hess, R., and Akert, K.: Zur Technik der Registrierung hirnelektrischer Erscheinungen im Rahmen des subcorticalen Reizversuches bei der Katze. *Helvet. physiol. et pharmacol. acta.* 9:316-325, 1951.
- ⁹⁷ Krakau, C. E. T.: An optical method of analyzing electroencephalographic and similar records. *EEG Clin. Neurophysiol.* 3:97-99, 1951.
- ⁹⁸ Leão, A. A. P.: The slow voltage variation of cortical spreading depression of activity. *EEG Clin. Neurophysiol.* 3:315-321, 1951.
- ⁹⁹ Lennox, M. A. and Robinson, F.: Cingulate-cerebellar mechanisms in the physiological pathogenesis of epilepsy. *EEG. Clin. Neurophysiol.* 3:197-205, 1951.
- ¹⁰⁰ Levinson, J. D., Gibbs, E. L., Stillerman, J. L., and Perlstein, M. A.: EEG and eye disorders. *Pediatrics.* 7:422-427, 1951.
- ¹⁰¹ Liberson, W. T.: Electroencephalography. *Am. J. Psychiat.* 107:510-514, 1951.
- ¹⁰² —, Henry, C. E., Scoville, W. B., and Whitcomb, B. B.: Observations on the effects of undercutting and cortical stimulation of the frontal and temporal lobes in man. *Proc. Eastern EEG Assoc. EEG. Clin. Neurophysiol.* In press.
- ¹⁰³ Liberson, W. T., Scoville, W. B., and Dunsmore, R. H.: Stimulation studies of the prefrontal lobe and uncus in man. *EEG Clin. Neurophysiol.* 3:1-8, 1951.
- ¹⁰⁴ Lilly, J. C.: Equipotential maps of the posterior ectosylvian area and acoustic

- I and II of the cat during responses and spontaneous activity. *Federation Proc.* 10:84, 1951.
- 105 — and Cherry, R.: Travelling waves of action and of recovery during responses and spontaneous activity in the cerebral cortex. *Proc. Am. J. Physiol.* In press.
- 106 Lloyd-Smith, D. L. and Henderson, L. R.: Epileptic patients showing susceptibility to photic stimulation alone. *Proc. Eastern EEG Assoc. EEG Clin. Neurophysiol.* 3:378-379, 1951.
- 107 L'organization des fonctions psychiques. Monnier, Brazier, Gemelli, Gonseth, Herrick, Klüver, McCulloch, Sherrington, Walter, Wiener. Editions du Griffon. Neuchâtel, Switzerland, pp. 103, 1951.
- 108 Marcus, R. W.: Hearing and speech problems in children. *Arch. Otolaryng.* 53:134-145, 1951.
- 109 Marshall, W. H. and Essig, C. F.: Relation of air exposure of cortex to spreading depression of Leão. *J. Neurophysiol.* 14:265-273, 1951.
- 110 — and Dubroff, S. J.: Relation of temperature of cerebral cortex to spreading depression of Leão. *J. Neurophysiol.* 14:153-166, 1951.
- 111 —, Landefeld, M., and Witkin, L. B.: Some aggregate functions of the cortical matrix. *Proc. Eastern Assoc. EEG. EEG Clin. Neurophysiol.* In press.
- 112 — and Witkin, L. B.: Components of striate reactions. *Am. J. Physiol.* meeting, Sept. 1951.
- 113 Marinacci, A. A., Rand, C. W., and Marinacci, H. K.: EEG findings in chronic subdural hematoma of infancy and early childhood. *Bull. Los Angeles Neurol. Soc.* 16:255-266, 1951.
- 114 Martin, P. and Cossa, P.: Signes électrographiques d'un cas d'hématome sous-dural. *Rev. neurol.* 84:671-676, 1951.
- 115 McLardy, T.: Diffuse thalamic projection to cortex: an anatomical critique. *EEG Clin. Neurophysiol.* 3:183-188, 1951.
- 116 Merlis, J. K., Grossman, C., Henriksen, G. F.: Comparative effectiveness of sleep and metrazol-activated electroencephalography. *EEG Clin. Neurophysiol.* 3:71-78, 1951.
- 117 Monnier, M. and Hufschmid, H. J.: Das Elektro-Oculogramm und Elektro-Nystagmogramm beim Menschen. *Helvet. physiol. acta.* 9:348-366, 1951.
- 118 —: Electroretinography with basal lead and without corneal electrode. *EEG Clin. Neurophysiol.* 3:241-244, 1951.
- 119 Morin, G., Gastaut, H., and Naquet, R.: Le cycle d'excitabilité des systèmes afférents corticaux chez le chat. *Rev. neurol.* 84:605-606, 1951.
- 120 Mundy-Castle, A. C.: Theta and beta rhythm in the electroencephalograms of normal adults. *EEG Clin. Neurophysiol.* 3:477-486, 1951.
- 121 Noel, G.: EEG et diagnostic des épilepsies. *Bull. Hôp. de Charlevoix*, 2:117-136, 1951.
- 122 Novikova, L. A. and Rusinov, V. S.: Basal-radial method for studying the electrical potentials of the brain in intracranial tumors. *Neuropath. & Psychiat. Moscow*, 20:51-59, 1951.
- 123 O'Flanigan, P. M., Timothy, J. I., and Gibson, H. G.: Further observations on the use of combined photic and chemically induced cortical dysrhythmia in psychiatry. *J. Ment. Sc.* 97:174-190, 1951.
- 124 Pampliglione, G.: Differences between the alpha rhythm and the responses evoked by photic stimuli, with particular reference to patients with visual field defects. *Proc. Soc. Italy, EEG, Bologna*, 1951.
- 125 Passouant, P., Cadilhac, J., and Latour, H.: Renseignements apportés par la

- stimulation auditive au cours du sommeil des épileptiques. *Rev. neurol.* 84:619-623, 1951.
- 126 —, Cadilhac, J., and Phillippot, M.: Rythmicité de petit mal au cours du sommeil, décharges rythmiques généralisées et localisées. *Rev. neurol.* 84:659-663, 1951.
 - 127 — and Salvaing, J.: Les signes électroencéphalographiques de la méningite tuberculeuse. Corrélations anatomo-électriques. *Rev. neurol.* 84:315-317, 1951.
 - 128 Pertuiset, B. and Capdeville-Arfel, G.: Deux techniques particulières d'exploration basale. Les électrodes sphéno-pterygoidiennes et orbitaires. *Rev. neurol.* 84:607-612, 1951.
 - 129 Petit-Dutaillis, D., Fischgold, H., Pertuiset, B., and Lairy-Boune, G. C.: Bases du traitement de l'épilepsie non tumorale par l'excision corticale. *Presse méd.* 65:1354-1360, 1951.
 - 130 Pine, I., Engel, F. L., and Schwartz, T. B.: The electroencephalogram in ACTH and cortisone treated patients. *EEG Clin. Neurophysiol.* 3:301-310, 1951.
 - 131 Pond, D. A. and Pond, M. H.: Glutamic acid and its salts in Petit Mal epilepsy. *J. Ment. Sc.* 97:663-673, 1951.
 - 132 Pribram, K.: Neurographic and behavior analysis of the frontal-temporal cortex of the monkey. *Proc. Eastern EEG Assoc. EEG Clin. Neurophysiol.* In press.
 - 133 Radermecker, J.: Les aspects électro-encéphalographiques dans les encéphalites de l'enfance. *Bull. Hôp. de Charleroi.* 2:137-150, 1951.
 - 134 Rémond, A.: Méthodes électroencéphalographiques d'enregistrement unipolaire et bipolaire (discussion). *Rev. neurol.* 84:580-584, 1951.
 - 135 Rémy, M.: Über die Anwendung der Elektrencephalographie in der Psychiatrie. *Schweiz. med. Wehnschr.* 81: 8 pp., 1951.
 - 136 —: Zur frage der photogenen epilepsie. *Monatschr. f. Psychiat. u. Neurol.* 121:230-239, 1951.
 - 137 Roger, A. and Gastaut, H.: A propos du seuil myoclonique de l'homme normal. *Rev. neurol.* 84:612-614, 1951.
 - 138 Romero, J. and Marshall, C.: Electrophrenic controlled hyperventilation for EEG activation. *EEG Clin. Neurophysiol.* 3:357-360, 1951.
 - 139 Roseman, E., Bloor, B. M., and Schmidt, R. P.: The EEG in intracranial aneurysms. *Neurology.* 1:25-38, 1951.
 - 140 Roth, M.: Changes in the EEG under barbiturate anesthesia produced by electroconvulsive treatment and their significance for the theory of ECT action. *EEG Clin. Neurophysiol.* 3:261-280, 1951.
 - 141 Schneider, J., Woring, E., Brogly, G., and Gloor, P.: Étude des variations de l'activité électrique du cortex cérébral et de certaines formations sous-corticales chez 37 chats soumis à l'influence des anesthésiques généraux usuels. *Rev. neurol.* 85:178-188, 1951.
 - 142 Schutz, E. and Muller, H. W.: Über ein neues zeichen zentralnervöser Erregbarkeitssteigerung im Elektrencephalogramm. *Klin Wehnschr.* 29:22-23, 1951.
 - 143 Schwab, R. S. and Abbott, J. A.: The clinical value of photic metrazol activation technique. *Proc. Eastern EEG Assoc. EEG Clin. Neurophysiol.* 3:378, 1951.
 - 144 Sherwood, S. L.: *Nature.* 169:157, 1952.
 - 145 Sloan, N., Pool, L. J., and Ransohoff, J.: ECG responses to electrical stimulation of peri-amygdaloid, anterior temporal, cingulate and orbital frontal cortices in non-epileptic man. *Proc. Eastern EEG Assoc. EEG Clin. Neurophysiol.* In press.
 - 146 Spiegel, E. A., Wycis, H. T., and Reyes, V.: Diencephalic mechanisms in petit mal epilepsy. *EEG Clin. Neurophysiol.* 3:473-475, 1951.

- 147 Starzl, T. E. and Magoun, H. W.: Organization of the diffuse thalamic projection system. *J. Neurophysiol.* 14:133-146, 1951.
- 148 —, Taylor, C. W., and Magoun, H. W.: Ascending conduction in reticular activating system with special reference to the diencephalon. *J. Neurophysiol.* 14:461-477, 1951.
- 149 —, Taylor, C. W., and Magoun, H. W.: Collateral afferent excitation of reticular formation of brain stem. *J. Neurophysiol.* 14:479-496, 1951.
- 150 Stephenson, W. A.: Intracranial neoplasm associated with fourteen and six per second positive spikes. *Neurology.* 1:372-376, 1951.
- 151 — and Gibbs, F. A.: A balanced non-cephalic reference electrode. *EEG Clin. Neurophysiol.* 3:237-240, 1951.
- 152 Stoll, J., Ajmone-Marsan, C., and Jasper, H. H.: Electrophysiological studies of subcortical connections of anterior temporal region in cat. *J. Neurophysiol.* 14:305-315, 1951.
- 153 Sullivan, J. F., Abbott, J. A., and Schwab, R. S.: The electroencephalogram in cases of subdural hematoma and hydroma. *EEG Clin. Neurophysiol.* 3:131-139, 1951.
- 154 Swank, R. L. and Brendler, S. L.: The cerebellar electrogram: effects of anesthesia, analeptics and local novocaine. *EEG Clin. Neurophysiol.* 3:207-212, 1951.
- 155 Thieffrey, S., Lérique-Koechlin, A., and Lérique, J.: Presentation of 3 EEG succesifs au cours d'une encéphalite subaigue, type van Bogaert. *Rev. neurol.* 84:684-687, 1951.
- 156 Thiry, S. and Farina, M.: Une nouvelle méthode d'enregistrement monopolaire en électroencéphalographie: la "detection push-pull." *Rev. neurol.* 84:584-588, 1951.
- 157 Titeca, J.: Le traitement médicamenteux de l'épilepsie. *Bull. Hôp. de Charleroi.* 2:185-200, 1951.
- 158 Tsukiyama, K.: Normal EEG and its development in the white rat. *M. J. Osaka Univ.* 3:15-20, 1951.
- 159 Ulett, G., Trufant, S., and Ronzoni, E.: The EEG with photic stimulation in psychiatric patients receiving ACTH. *EEG Clin. Neurophysiol.* 3:79-81, 1951.
- 160 Van Harreveld, A. and Stamm, J. S.: On the conditions for the recording of Leão's spreading depression. *EEG Clin. Neurophysiol.* 3:323-328, 1951.
- 161 Verzeano, M.: Servo-motor integration of the electrical activity of the brain and its applications to the automatic control of narcosis. *EEG Clin. Neurophysiol.* 3:25-30, 1951.
- 162 Vogel, T. and Walter, W. G.: Discussion sur les bases mathématiques de l'analyse de fréquence. *EEG Clin. Neurophysiol.* 3:435-442, 1951.
- 163 Walker, A. E.: The treatment of epilepsy by cortical excision. *J. Pediat.* 38:285-298, 1951.
- 163a Wall, P. D., Fry, W. J., Stephens, R., Tucker, D., and Lettvin, J. Y.: Changes produced in the central nervous system by ultrasound. *Science.* 114:686-687, 1951.
- 164 Walter, W. G.: Discussion on recent advances in the EEG diagnosis of epilepsy. *Proc. Roy. Soc. Med.* 44:315-322, 1951.
- 165 —: Activity patterns in the human brain. *In: Aspects of Growth and Form.* Ed. L. L. Whyte, New York, Pellegrini, 1951.
- 166 — and Shipton, H. W.: A toposcopic display system applied to neurophysiology. *J. Brit. Inst. Rad. Eng.* 260-273, July, 1951.

- ¹⁶⁷ — and Shipton, H. W.: A new toposcopic display system. *EEG Clin. Neurophysiol.* 3:281-292, 1951.
- ¹⁶⁸ Weil, A. A.: Electroencephalographic findings in post-traumatic encephalopathy. *Neurology* 1:293-298, 1951.
- ¹⁶⁹ Williams, D.: Clinical electroencephalography. Chapter 19. *In: Modern Trends in Neurology*. New York, Hoeber, 1951.
- ¹⁷⁰ Woring, M., Schneider, J., Brogly, G., and Gloor, P.: Aptitude relative des divers anesthésiques généraux usuels à la pratique de la corticographie. *Rev. neurol.* 84:625-629, 1951.
- ¹⁷¹ Wyss, O. A. M.: Eléments physiologiques de l'électroencéphalogramme. *J. suisse de méd.* 8:175-193, 1951.

Cerebrospinal Fluid

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COMPLICATIONS OF LUMBAR PUNCTURE. In order to prevent headaches after lumbar puncture, Dripps et al.⁴¹ and Hart et al.⁵⁴ advise to minimize the local trauma, to make only one hole in the dura, to use pencil point needles and to keep the patient immobile during the puncture. Glesne⁴⁹ measured the lumbar pressure in 20 patients with headaches after puncture and found lower values than in controls; the author infers that leakage may be the cause of the headaches. Paralysis of the external rectus muscle as reported by Goodall⁵² may be due to the lessening of the cushioning effect of the cerebrospinal fluid (CSF) that affects the abducens nerve. (Adelman and Lyons.⁴) Rice et al.¹¹² alleviate post-spinal headaches by peridural and subarachnoid injections of saline solution. Gloz⁵⁰ suggests the use of ultrashortwaves in order to raise the CSF pressure.

More serious sequelae are reported following *spinal anesthesia*. Dripps differentiates the action of the puncture from that of the anesthetic. According to Rabiner¹⁰⁸ the changes are of meningeal character. Effron et al.⁴⁴ add 12 new cases of grave paralysis to 3 formerly reported. Dwyer⁴² lists the following reasons for complications: uncontrolled height of the anesthesia, sudden peripheral circulatory failure, intramuscular injection, drug sensitivity, direct action of the drug on medullary centers.

Anatomy and Physiology. According to Bertrand et al.,²⁰ the choroid plexus does not play an important role in the hypersecretion of CSF. Aloff⁸ doubts that the CSF circulates through the substance of the brain either from the ventricles and along the perivascular spaces to the subarachnoid spaces or in the opposite direction. The circulation of the CSF is markedly influenced by the cavity system of the sinus which exercises a suction with each inspiration of the thorax (Kiss⁷¹). In 38 cases of closed cerebral trauma, Reimers et al.¹¹¹ found the reabsorption of the CSF inhibited while only some cases showed retardation of the secretion. Acceleration of the latter is only very rarely observed.

Various methods have been described for the study of complete and partial *block* of the CSF pathways. Lorber⁹⁰ uses either penicillin or air injection. By using penicillin injections in 55 cases, 23 blocks could be

detected, 18 within the spinal theca. This method proved to be superior in tuberculous meningitis to determinations of the lumbar protein content or of the ratio lumbar: cisternal protein. The penicillin method is useful only in complete block, but fails in the detection of tentorial block, partial obstruction, exudate or tumor. 100 pneumoencephalograms⁹¹ were performed partly to obtain a more complete understanding of the circulation of the CSF in tuberculous meningitis; subarachnoid air was absent in tentorial or basal cisternal block. In three cases, this sign preceded the hydrocephalus. When subarachnoid air was present, hydrocephalus was seen in four children only. Aird et al.⁷ describe in absorptive block the triad of small or obliterated subarachnoid spaces, large "normal" or dilated ventricular spaces, and delayed absorption of ethylene gas, following its pneumoencephalographic injection. From findings in 630 cases (tumors, meningoencephalitis and some epileptics) the authors conclude that a delayed absorption of injected gas is a relatively sensitive test of a partial obstructive process preceding an impairment of the CSF circulation with consecutive increase in intracranial pressure.

The influence of inhaled CO₂ of various concentrations upon CSF pressure has been studied by Goldensohn et al.⁵¹ The maximal effect is reached within 5 minutes. No direct correlation between increase in CSF pressure and either arterial or venous pressure was observed. Venous blood pH shows decreases not exceeding 0.07–0.25 units. Excessive increases of CSF pressure (up to 300 mm H₂O) have been reported by Horwath⁵⁹ in a case of barbiturate idiosyncrasy. Beynon²¹ discusses the possible effect of streptomycin in increasing intracranial pressure. The influence of vascular hypertension upon the CSF pressure was studied in 149 cases by Kubik et al.⁷⁶ The CSF pressure was 200 mm or above in 40 cases. There was a direct relation between the occurrence of papilledema and the level of the CSF pressure. No correlation between the latter and the severity of the headaches could be established. Hypotension of the CSF due to central disturbances should, according to Lembcke,⁸⁰ be treated by constant fluid intake.

Various modifications of the Queckenstedt test have been suggested. Longo et al.⁸⁹ record the changes of CSF pressure graphically while the seated patient gradually extends the head from the position of flexion to maximal hyperextension. Kaplan et al.⁶⁵ propose manual bilateral jugular compression with the head in each of three positions (midposition, full flexion and full extension). Manometric abnormality in only one position seems to be pathognomic. It is suggested that the anomalous manometric and biochemical findings are the results of intermittent occlusion of the spinal circulation, depending upon head posture.

Constituents of the CSF. In order to obtain normal values, Neel⁹⁹ has performed 1520 protein determinations and 518 cell counts on CSFs col-

lected during spinal anesthesia. While differences between the sexes were only minimal, it is of great interest that even chronic and localized intra-abdominal inflammations produce slight variations of the CSF. The value of divided samples has been established chiefly in serologic studies (Koch⁷²).

Inorganic ions. In systematic studies on dogs, Leusen⁸² ascertained the influence of the pH in the CSF on respiration. Lowering of pH stimulated respiration, elevation of pH made it slower and more irregular. Hyper-ventilation produced progressive alkalosis in both blood and CSF. Acidosis produced by inhalation of 10 per cent CO₂ caused parallel pH lowering in both fluids. Fluids of various pH (from 7.0 to 7.5) infused into the cerebral ventricles produced similar changes in the blood. In normal conditions the pH variations of the CSF⁸³ are parallel and secondary to those of the blood. On the other hand, the independent pH variations of the CSF in meningitis may have an appreciable effect on respiration.

By modifying an old procedure, Urban et al.¹²⁴ reduce the error in Na determinations to less than 2 to 3 per cent. According to Koeigstein,⁷⁴ 1 to 2 mg KCl cisternally injected into cats approximately doubles the CSF K and elicits scratching attacks. Administration of morphine, picrotoxin, NH₄Cl, pilocarpine and caffeine in quantities sufficient to produce scratching is accompanied by an increase of the CSF K, sometimes up to 100 per cent. The K increase in serum is smaller and slower. Ca reduction has a similar effect. Reestablishment of the normal Ca/K ratio alleviates the attacks caused by K excess. Mg may be substituted for Ca. Increase of the K level in the CSF up to 1 g/liter produces increased stomach motility in normal dogs but has the opposite effect in dogs with inherent hypermotility and dogs under action of pilocarpine. Increase of either CaCl₂ or MgCl₂ suppresses gastric motility, but only the absence of CaCl₂ produces hypermotility. Simultaneous increases of KCl to 1.77 and of CaCl₂ to 1.0 g/liter neutralize each other. Section of the vagi abolishes the effects of either high K or low Ca concentrations in the CSF. According to Münch-Petersen,⁹⁸ the copper content of the CSF varies from 3 to 25 per cent. Age, clinical conditions, blood and Cu level seem to be without influence on these figures.

The detection of Fe⁺⁺⁺ in one drop of CSF has been studied by Berisso¹⁹ who used various microchemical methods. Lehman et al.⁷⁹ report the Fe content of CSFs in 98 psychiatric patients. Statistically significant differences seem to exist between acute and deteriorated schizophrenics, and between organic psychoses and acute schizophrenia. It is suggested that a low iron content of the CSF may reflect reduced cellular activity of the brain tissue.

Trautman et al.¹²³ explain high chloride content of the CSF by selective filtration out of the CSF system. A rapid microdetermination of chlorides

in CSF is described by Franco.⁴⁸ It includes a treatment with $\text{Ba}(\text{OH})_2$ and ZnSO_4 and centrifugation and titration of the filtrate with 0.02 N AgNO_3 to a pink color with dichlorofluorescein as an indicator.

Crystalline forms of oxalic, carbonic, and phosphoric acid salts have been found in some of the 1700 CSFs which Corbino³⁴ has studied using a special technic. Pathologic fluids contain these crystals in a relatively high amount. Formation of crystals originating in cystic brain tumors is mentioned. Their appearance in the CSF after its withdrawal is probably due to changes in pH due to loss of CO_2 .

Organic substances. The *carbohydrates* of 57 normal CSFs have been investigated by paper partition chromatography, and the presence of glucose, fructose and glucosamine in the free state has been established (Eastham et al.⁴³). The total reducing substances ranged from 66 to 112 mg/100 ml (mean 88), or from 35 to 90 mg/100 ml (mean 67) according to the method employed. The fructose concentration ranged between 1.6 to 7.2 mg/100 ml (mean 3.8). The analogous values for glucosamines are 9 to 16 mg/100 ml (mean 11). There is also evidence for the occasional existence of other keto sugars and for pentoses. A practical method for determining small amounts of glucose in 0.5 ml of CSF has been described by Escarza,⁴⁵ who precipitates the proteins with picric acid solution, heats the filtrate with 20 per cent NaOH and compares the color with that of a similarly treated glucose standard. Carrara,²⁸ using the Crecelius-Seifert method, reports a glucose concentration of 0.045 to 0.065 per cent in normal CSFs, 0.075 to 0.1 per cent resp. in encephalitic Parkinsonism; and 0.065 to 0.075 in Parkinson's disease. In 30 cases of diabetes mellitus, Tortolini¹²² finds 54 to 210 mg per cent glucose with no definite relation to the blood sugar values. The diagnostic and prognostic value of CSF sugar values has been studied by a number of authors in various conditions. In tuberculous meningitis, Sedallian et al.¹¹⁵ find in patients with isolated acute lymphocytic meningitis a low sugar content of the CSF (less than 0.04 gm/100 ml) early enough to be of diagnostic value. In tuberculous meningitis complicated by tuberculosis of other organs, by miliary tuberculosis and associated initially with neurologic symptoms, the drop in CSF sugar occurs too late to be of diagnostic value. Prognostically very low values indicate the gravity of the condition; return to normality within 3 to 5 months speaks for the efficacy of the treatment. (See also tbc. meningitis.) Persistently low values warn against discontinuation of intraspinal treatment. A return of the CSF sugar values to normal is an indispensable indication of recovery; however, it is not sufficient evidence alone to justify complete discontinuation of streptomycin. According to McCrumb et al.,⁹⁴ patients affected with *Hemophilus influenzae* meningitis responding favorably to antibiotics show a steady rise of the CSF sugar values.

Urea. Normal values, according to Lickint,⁸⁶ range from 7.4 to 16 mg/100 ml. These values were 71 to 90 per cent of the corresponding concentrations in the blood sera. In a number of neurologic conditions, with the exception of hydrocephalus and meningitis, Lickint reports normal values. Barucci¹⁶ finds in the CSF of patients with nervous diseases 0.014 to 0.033 per cent, mostly 0.020 to 0.027 per cent. But his blood:CSF ratios are similar to the ones mentioned by Lickint.

Uric acid. For the determination of uric acid, Praetorius¹⁰⁵ uses the difference in the extinction coefficients at 290 to 295 μ before and after the addition of uricase. Deproteinization is not necessary. The reproducibility is about ± 3 per cent.

Determinations of *pyruvic* and *lactic acid* were made in early and later stages of tuberculous meningitis (Abe et al.³). The average values in mg/100 ml were 3.13 and 4.41 for pyruvic and 29.9 and 52.0 for lactic acid. Amatuzio et al.⁹ find pyruvic acid increased in the CSF of patients with hepatic coma. In psychiatric cases subjected to *electroshock* the lactic acid frequently (and the pyruvic acid less often) shows an increase in both CSF and blood. Similar results were found after muscular work. (DeFranciscis et al.³⁶) The method of Caselli and Ciaraufi showed 0.28–26.97 mg/100 ml *acetic acid* (Kemali⁶⁷) in normal and pathologic fluids. A colorimetric determination of acetone bodies in the CSF is described (Kodama et al.⁷³). This reaction is positive with acetone and acetoacetic acid but negative with β -hydroxybutyric acid. Histamine determinations in the human CSF and in the aqueous humor have been made by Corrado³⁵ using a standard guinea pig ileum method. Values of 0.025 γ /ml and 0.055 γ /ml respectively were reported.

Amino acids. According to Kemali,⁶⁶ ascending unidimensional chromatography shows the presence of alanine in the CSF. *Residual Nitrogen* (RN) determinations in the CSF (Lickint⁸⁷) gave normal values ranging from 12 to 19 mg/100 ml. They were about 42 per cent below the corresponding values in the blood serum. In a study of 139 patients, hydrocephalus, cerebral concussion, encephalitis, eclampsia and neurosyphilis gave, in most instances, normal values. In meningitis, both normal and high RN values were found. Large increases occurred in kidney diseases. The determination of creatinine, uric acid, amino acids, xanthopterin or indican cannot be substituted for determinations of RN because these substances vary independently.

Protein. Some of the following findings may be of diagnostic interest. In a near lethal phenobarbital poisoning the CSF showed a positive Pandy test and a total protein content of 112 mg/100 ml.⁹⁵ Of 12 samples of CSFs from persons treated with tuberculin, 8 showed microclots after addition of thrombin; similar clots were present in 9 of 20 control samples. The

CSF plasminogen level of tuberculous persons varied from 8 to 256 Christensen units/ml (Fletcher⁴⁷). In a six-weeks-old child treated because of *Focalis alcaligenes meningitis* with cisternally injected streptomycin, a protein increase was noticed which persisted over 23 weeks. No ill effects were noticed clinically after $2\frac{1}{2}$ years (Beynon²¹). Similar observations were made in patients with tuberculous meningitis treated with streptomycin and observed for $2\frac{1}{2}$ to $3\frac{1}{2}$ years (Calnan et al.²⁷). In 23 cases of severe rheumatoid arthritis high total protein and globulin levels in the CSF, and high globulin: albumin ratios were recorded. A correlation of these findings seems to exist with the protein content of the serum but not with clinical findings (Lush et al.⁹³). In Kubik's⁷⁶ hypertensive patients, 69 per cent of cases with elevated protein had values between 51 and 100 mg/100 ml. Protein was elevated more frequently in cases with increased CSF pressure and papilledema. The decrease in protein in the CSF after pneumoencephalography (Bickerstaff²²) is explained by dilution of lumbar with intracranial and cisternal fluid.

In a number of papers, the technics of *protein determinations* and their results are the chief topic. Gross⁵³ has checked turbidimetric, biuret and tyrosine equivalent methods with micro Kjeldahl determinations. While the two latter methods checked with the N-determination within ± 6 mg/100 ml, the sulfosalicylic acid turbidity did not give reproducible results if the protein content exceeded 70 mg/100 ml. With the permanent Perspex standards, King⁷⁰ achieved with the sulfosalicylic turbidimetric procedure protein estimation with a ± 10 per cent accuracy. Comparative photoelectric determinations of opalescence caused by (1) sulfosalicylic, (2) trichloroacetic, and (3) K-ferro cyanide acetic acid, show, according to Heepe et al.,⁵⁵ that the 1st and 3rd substance produce a greater stability of opalescence, while in number 3 the opalescence is independent of the dispersion of the precipitated protein. While the above methods deal with determination of the total CSF protein, the Kunkel zinc sulfate test as performed by Donovan et al.³⁹ seems to remove the γ -globulins from the CSF. (1 ml CSF is added to 1 ml of a 0.005 M solution of ZnSO_4 brought to a pH of 6.9–7.1 by a barbiturate buffer. The test is read 4 hours after mixing, on a 0–4+ basis. Two plus or higher is considered positive.) The test shows a high degree of correlation with the colloidal gold test. Nineteen out of 20 proven cases of multiple sclerosis gave a positive test. According to Saifer,¹¹³ the cephalin-cholesterol flocculation test (modified Hanger method) when above 3 units, also indicates an increase of γ -globulin and fibrinogen. Corrections of total protein estimations in hemorrhagic CSFs have been computed by Badoux.¹² He established experimentally that 1,000 red blood cells originating from blood of normal cell count correspond to a protein increase of 0.0095 g/l. in the CSF. This cor-

rection is only feasible if the number of the red cell in the CSF is between 2000–100,000 per cu. mm. The correction is then subtracted from the total protein content of the CSF.

A number of authors use *electrophoresis* for the study of CSF proteins. The use of various apparatus and methods explains, at least partly, the differences in results. While Schneider et al.¹¹⁴ find that the albumin/globulin ratio in normal CSF is similar to the one in serum, Labhart et al.⁷⁷ find it somewhat higher. According to Schneider, corresponding CSF and serum components have similar electrophoretic behavior. But Fisk et al.⁴⁶ found in 65 CSF specimens a protein which migrated 1.3 times faster than albumin, showed a similar sedimentation as the latter and formed 9 per cent of the total protein. In nine cases, two rapidly migrating components were observed. Booy²⁴ found in 50 cases that with normal protein concentration albumin was always present but globulin not always demonstrable. If the total protein content was increased, globulin β and γ could be identified but globulin α was not demonstrable. According to Labhart, the albumin-globulin ratio in the CSF is lowered in meningitis; in lymphocytic (virus?) meningitis, there is a marked increase of γ -globulins. There is no definite relation between the results of the Pandy and colloid reactions and of electrophoresis.

Under pathologic conditions and under the influence of treatments, a variety of reactions and substances can be detected in the CSF. Janbon et al.⁶² report a high fat content (5 g/1000 ml) as a transitory finding in the acute stage of optic neuromyelitis. Kent and Neurath⁶⁸ find the anti-complementary properties of CSF normally minimal. In a human case of torulosis, Neill et al.¹⁰⁰ describe in the CSF serologically reactive substances detectable by specific precipitation and by complement fixation. These reactive substances are heatstable and are probably capsular polysaccharides of the fungus. Agostini⁵ finds a reticulocytogenic factor in the CSF of rabbits after bleeding. According to Stefanini et al.,¹²¹ phlogogenic substances were found in the CSF of seven cases of multiple sclerosis out of eight, in four cases of chorea minor out of five, and in three cases of epilepsy out of six. Abe et al.¹ have observed a decrease of thiamine in prelethal cases of tuberculous meningitis, in improving cases 6.6 to 16 γ per cent thiamine (average 10.9 γ per cent) was found. Hyperpiesin and miopiesin, principles occurring in the pituitary gland, were traced by Dietz et al.³⁸ in the CSF.

There is only very little or no *procaine esterase* in the CSF contrary to plasma (Aven et al.¹¹). According to Helrich et al.⁵⁶ procaine is absorbed into the systemic circulation where it is metabolized. *Cholinesterase* was absent in the CSF of 18 schizophrenics (Barbato¹⁴) but appeared together with a slight protein and cell increase in 14 cases 24 hours after intralumbar

injection of 2 ml H₂O. *Lysozyme* activity is found only in some pathologic CSFs. It is not in normal CSFs either of adults or children, according to Rabe but only in inflammatory diseases of the CNS (Poggiali,¹⁰⁴ Rabe et al.¹⁰⁷). The highest titers of lysozyme were found in patients with purulent bacterial meningitis, also in the absence of pleocytosis. It is suggested to use lysozyme in certain instances as a sensitive index of inflammatory disease involving the CNS.

Drugs. The intensive use of antibiotics is reflected in a number of papers dealing with the quantitative and qualitative determination of these substances in the CSF. *Penicillin* levels after intramuscular injections of commercial procaine penicillin (600,000 units) were determined by Wright et al.¹³⁰ between 2 and 290 hours after injection. After 31 hours the level was 82 per cent and 91 per cent after 122 hours. Redfearn et al.¹¹⁰ also find bactericidal penicillin levels in the CSF in 70 per cent of their patients, after administering a single dose of 0.5 mega units. Diseases causing excess of protein in the CSF, higher age of the patients, cerebral gliomatous cysts increase the permeability of the blood-CSF barrier to penicillin. In *Hemophilus influenzae* meningitis treated successfully with *Chloramphenicol*, levels ranging from 5 to 50 $\mu\text{g/ml}$ were reached in the blood, and 5–25 $\mu\text{g/ml}$ with a mean average of 10 μg in the CSF (McCrumb⁹⁴). Also *acidione* administered intravenously passes into the CSF in amounts able to inhibit the growth of *torula* (Wilson et al.¹²⁹). Whitlock et al.¹²⁷ adapted their turbidimetric method used for aureomycin to the assay of chloramphenicol, penicillin, streptomycin and terramycin in the CSF.

Physicochemistry. The use of combined ultraspectrophotometrical and chemical methods has been continued by various authors. (See Volume VI, 1951, of the *Progress* series.) Séguin¹¹⁷ studied CSF of 34 schizophrenics and 17 normal individuals. The ultraviolet absorption was measured and corrected for the protein content of the CSF. At a wave-length of λ 268 m μ the mean absorption for the schizophrenic group is 0.799 ± 0.040 , while the analogous values for the normal group are 0.668 ± 0.023 . The differences are statistically significant. These results are in close agreement with similar ones published by us in 1948. Sophian et al.¹¹⁸ on the one hand confirm the results of Spiegel-Adolf et al.¹²⁰ that the content of ascorbic acid and albumin can account for the character and intensity of the ultraviolet absorption spectrum of fresh normal CSF. On the other hand, they were unable by using spectrophotometry before and after alkaline destruction of ascorbic acid (Strait et al.) to correlate their results with the ones obtained by the 2,6-dichlorophenolindophenol colorimetric determination of this substance. Preliminary findings with combined ultraspectrographic and chemical methods in brain tumors (Spiegel-Adolf and Wycis¹¹⁹ have been reported in the preceding *Progress*. Further attempts by the same

authors using these methods to differentiate the CSFs of 52 brain tumors seem to indicate that the ultraspectrographical values corrected for protein and ascorbic acid are significantly higher in gliomas and meningoendotheliomas than in metastatic carcinomas of the brain. A comparison between the CSF values in brain tumor cases and the data for the corresponding tumor extracts points to a possible influence of the location of the tumor (vicinity of the subarachnoid space) and of its metabolism upon the extent of CSF changes.

Colloid Reactions. From comparative studies (767 specimens, 647 patients), Ingerslev⁶¹ concludes that the Riebeling hydrochloric acid collargol reaction cannot replace Bisgaards reaction and cell count.

Microscopic Studies. In experimental studies in dogs, Bedford¹⁷ found that 24 hours after intracisternal injection of distilled water, Ringer solution and isotonic NaCl the cell count increased in the above sequence. It seems, therefore, that in the preparation of isotonic solutions for subarachnoid injections, the use of simple NaCl to render the solutions isotonic is not advisable. Lorber⁹¹ noticed increase of cells after air injection. The increasing use of antibiotics in meningitis of various origin has enhanced the value of bacteriologic studies, e.g., of the disappearance of bacteria as a therapeutic indicator (McCrumb⁹⁴). If bacteria have been destroyed and disappear from the CSF, some of their chemical components can still be traced; this method can be used for diagnostic purposes. Larson⁷⁸ finds capsular polysaccharides in five cases of pneumococcus meningitis and in one case of Klebsiella pneumoniae demonstrable in the CSF two to eight days after the disappearance of the organisms. The type of bacteria present in pathologic CSFs often determines the kind of treatment to be used, e.g., according to Aguilo et al.⁶ sulfathiazol and penicillin are advisable in pneumococcus meningitis, sulfathiazol and streptomycin in meningitis caused by Pfeiffer's bacillus.

A rather new method for the isolation of tubercle bacilli in the CSF has been described by Kang et al.⁶⁴ Starting from the observation that, contrary to other bacilli, tubercle bacilli in an electric field migrate to the cathode, the authors have used an electrolytic method in 11 cases suspected of tuberculous meningitis. In all CSFs tested by this method, the outcome was positive, whereas in none tubercle bacilli had been detected by direct smear and culture methods and only 6 had been positive by the concentration method.

CSF Syndromes

Encephalitis. Mendelsberg⁹⁶ describes a fulminant case which ultimately recovered with relatively unaltered CSF. Hullinghorst et al.⁶⁰ give a survey of the CSF findings during the Japanese B encephalitis epidemic in Korea

in 1949. The cell count showed an average of 200 cells with the lymphocytic elements averaging 80 per cent. Chlorides were 320 to 473 mg/100 ml, glucose was normal or moderately increased, Pandy positive. Calcium values (Cart-Collip method) frequently were reduced from the normal range of 7 to 8 mg to 5 to 5.5 mg/100 ml.

Poliomyelitis. Nicholls et al.¹⁰¹ studied 320 cases; CSF changes could not be found in 13.8 per cent.

Acute Disseminated Encephalo-Myelitis. Kabat et al.⁶³ produced this condition in rhesus monkeys by the injection of brain emulsions with adjuvants. In the acute phase of the disease, a characteristic rise of the cell count, total protein and γ -globulin is reported with or without changes of the percentage of the latter in relation to the total protein. As the acute process subsides, the total protein declines and increases in the ratio of γ -globulin to total protein become frequent.

Multiple Sclerosis. Protein exceeded 45 mg/100 ml in 36 per cent of the cases (Von Storch et al.¹²⁵), but according to Lotmar,⁹² is usually about 50 mg/100; 75 to 100 mg/100 are exceptional. A single case of 278 mg/100 is explained by the size of the lesion and its location beneath the ventricular ependyma.

Von Storch finds more than 10 cells in 8 per cent of his cases; Müller⁹⁷ observes a correlation of the cell count and fresh clinical recurrences. The colloid gold reaction shows a type D curve of three grades of intensity according to Von Storch in 158 cases; he accepts a strong D reaction as confirming evidence of multiple sclerosis. On the other hand, Müller finds that the mastic reaction in the majority of cases remains unchanged for about $3\frac{1}{4}$ years and that the precipitation occurs independently of the clinical picture, degree and duration of the disease.

Meningitis. In a case of aseptic meningitis (Swineherd's disease) due to *Leptospira Pomona*, Coffey et al.³¹ report 980 cells per cu. mm. of which 86 per cent were lymphocytic and 14 per cent neutrophils. Protein content was 98 mg/100 ml., the initial pressure 280 mm. In experiments on cats, Zubrod¹²² used *Klebsiella pneumoniae* to produce meningitis. Such cats only survived in which the streptomycin concentration of the CSF reached sufficient heights. From the very extensive literature on *tuberculous meningitis* only the following points related to CSF will be mentioned. According to Brainerd et al.²⁵ an early return of glucose to normal is sometimes only transient, a later relapse should be a signal for intrathecal therapy. Sedallian et al.¹¹⁶ mention that even in patients apparently cured of tuberculous or other lymphocytic meningitis the passage of glucose into the CSF is delayed, but it is accelerated after suppurative meningitis. Organisms disappear later than glucose changes. Büscher²⁴ advises thorough CSF investigations in cases with focal syndromes. The recent polarographic studies

of Homolka et al.⁵⁸ seem quite promising; according to the authors' studies on 525 specimens from 218 patients, polarography permits a differentiation of tuberculous meningitis with 97.5 per cent of probability. The prognostic value of microscopic and guinea pig tests has been emphasized by Kornushenko et al.⁷⁵ Twelve out of 16 cases of tbc. meningitis recovered in which the CSF became sterile after streptomycin treatment. In the remaining cases with infectious CSF, recurrences occurred, two of them fatal. In cases under treatment with streptomycin, CSF studies have become a valuable help. Lorber⁹¹ advises to use pneumoencephalograms (see above) for selection of cases for treatment or abandonment of treatment. The latter should be continued until the CSF becomes sterile (De Toni³⁷). Abe et al.² report in agonal stages changes in glucose, pyruvic acid and lactic acid. While the first shows a decrease, the other two increase in comparison with earlier stages of the disease. The shortest time for a return of the CSF to normality (45 mg. sugar, 40 mg. or less protein and 4 or less cells per cu. mm.) after streptomycin treatment is, according to Cathie et al.,²⁹ 12 months.

Persistence for many months of cell and protein increase and decrease of chlorides is reported by others (Brainerd,²⁵ Cathie²⁹). Important for a correct evaluation of the CSF findings in streptomycin treated cases are the following observations. Cohen et al.³² report that 0.1 grams streptomycin given intrathecally causes an irritation of the meninges with temporary cell and protein increases. According to Williams,¹²⁸ sterility of the CSF induced by streptomycin does not prevent eventual death of the patient from mechanical reasons; early and fast treatment is therefore advised. Nevertheless, the pathologic studies of Levinson et al.⁸⁵ seem to speak against intrathecal treatment as the healing starts around smaller blood vessels and not where free contact with the streptomycin laden CSF exists.

REFERENCES

- ¹ Abe, M., Nagashima, Y., and Tajima, Y.: Clinical physiological studies on carbohydrate metabolism. II. CSF in the early stages of tuberculous meningitis. *Igaku to Seibutsugaku*, 18:27, 1951.
- ² —, Sugawara, T., and Nagashima, Y.: Clinical physiological studies on carbohydrate metabolism. IV. Changes in the CSF at the critical stage of tuberculous meningitis. *Igaku to Seibutsugaku*, 18:190, 1951.
- ³ —, Sugawara, T., Nagashima, Y., and Tajima, Y.: Changes in the CSF in tuberculous meningitis. *Igaku to Seibutsugaku*, 18:101, 1951.
- ⁴ Adelman, M. H. and Lyons, S. S.: Abducens nerve palsy following spinal anesthesia. *J. Mt. Sinai Hosp.* 17:1055, 1951.
- ⁵ Agostini, L.: The presence of a reticulocytogenic factor in the CSF. *Riv. biol.* 42:339, 1950.
- ⁶ Aguilo, C. and Meneghello, J.: Treatment of purulent meningitis in infants without use of intraspinal route. *Rev. chilena de pediat.* 21:486, 1950.

- ⁷ Aird, R. B. and Zeale, D.: Pneumoencephalographic study of CSF absorptive-block mechanisms. *Arch. Neurol. & Psychiat.* 66:199, 1951.
- ⁸ Aloff, I. A.: The movements of the cerebrospinal fluid through the brain along the perivascular spaces. *Vopr. neyrokhir.* 6:12, 1950.
- ⁹ Amatuzio, D. S. and Nesbitt, S.: Study of pyruvic acid in blood and spinal fluid of patients with liver disease with and without hepatic coma. *J. Clin. Investigation.* 29:1486, 1950.
- ¹⁰ Aquilina, Joseph T.: Tuberculous meningitis cured with streptomycin. *J.A.M.A.* 147:564, 1951.
- ¹¹ Aven, M. H. and Foldes, F. F.: Hydrolysis of procaine and 2-chloroprocaine in spinal fluid. *Federation Proc.* 10:158, 1951.
- ¹² Badoux, V.: The correction of total protein estimations in haemorrhagic cerebrospinal fluids. *Schweiz. med. Wchnschr.* 81:85, 1951.
- ¹³ Baptista Dos Reis, J. and Lemmi, O.: Causes of failure in the collection of cisternal or lumbar CSF. *Arch. Neuro-psiquiat., S. Paulo.* 8:182, 1950.
- ¹⁴ Barbato, L.: Cholinesterase of CSF and the mesoectodermal barrier. II Pisani. 63:41, 1949.
- ¹⁵ Barth, E.: Speransky's CSF pump and its therapeutic application. *Deutsche Gesundheitswes.* 5:392, 1950.
- ¹⁶ Barucci, M.: Ratio of urea in the blood and CSF (of pts. with nervous diseases). *Riv. di pat. nerv.* 71:199, 1950.
- ¹⁷ Bedford, T. H. B.: Cell content of CSF. *Brit. J. Pharmacol.* 3:80, 1948.
- ¹⁸ Beakaert, J.: The influence of the level of potassium, calcium, and magnesium in cerebrospinal fluid on gastric motility. *Arch. internat. de physiol.* 58:69, 1950.
- ¹⁹ Berisso, B. and Bruno, A. A.: Microchemical study of cations and anions in spinal fluid. *Pubs. inst. invest. microquim., Univ. nacl. litoral.* 13:13, 1949.
- ²⁰ Bertrand, L. and Salvaing, J.: The choroid plexuses in meningeal tuberculosis. *Presse méd.* 59:230, 1951.
- ²¹ Beynon, D.: Prolonged abnormality of CSF after cisternal streptomycin. *Lancet.* 1:322, 1951.
- ²² Bickerstaff, E. R.: Changes in the CSF during pneumoencephalography. *Lancet.* 259:683, 1950.
- ²³ Blanch, P. C., Scremini, A. P., and Katz, E.: Tuberculous meningitis cured by streptomycin. *Arch. de pediat. d. Uruguay.* 22:18, 1951.
- ²⁴ Booy, J.: Electrophoresis in cerebro-spinal fluid-proteins. II. *Folia psychiat. Amsterdam.* 53:502, 1950.
- ²⁵ Brainerd, H. D. and Eagle, H. R.: Effect of streptomycin on tuberculous meningitis. *Ann. Int. Med.* 33:397, 1950.
- ²⁶ Büscher, H. K.: Focal syndrome in tuberculous meningitis. *Beitr. klin. Chir.* 181:61, 1950.
- ²⁷ Calnan, W. L., Rubie, J., and Mohun, A. F.: Tuberculous meningitis treated with streptomycin.: Follow-up of survivors for a minimum of 2½ years. *Brit. M. J.* 1:794, 1951.
- ²⁸ Carrara, E.: Glucose of CSF in Parkinson's syndrome. *Riv. pat. nerv.* 71:162, 1950.
- ²⁹ Cathie, I. A. B. and McFarlane, J. C. W.: Adjuvants to streptomycin in treating tuberculous meningitis in children. *Lancet.* 2:784, 1950.
- ³⁰ Choremis, C., Zervos, N., Pantazis, S., et al.: Further observations on application of streptomycin in treatment of tuberculous meningitis in the Athens Univ. *Ped. Clin. Acta Tuberc. Scandinav.* 25:8, 1950.

- ³¹ Coffey, J. H., Dravin, I., and Dine, W. C.: Swineherd's disease (aseptic meningitis) due to *leptospira pomona*. *J.A.M.A.* 147:949, 1951.
- ³² Cohen, S. and Gans, R. H.: Treatment of tuberculous meningitis with streptomycin. *Dis. of Chest.* 18:215, 1950.
- ³³ Conner, E. H. and Dripps, R. D.: Use of lucaine in study of spinal anesthesia. *Anesthesiology.* 11:686, 1950.
- ³⁴ Corbino, D.: Crystals in the cerebrospinal fluid. *Riv. neurol.* 20:1, 1950.
- ³⁵ Corrado, M.: Relation between histamine concentrations in the aqueous humor and the CSF. *Ann. ottal. e clin. ocul.* 75:33, 1949.
- ³⁶ DeFranciscis, P. and Lampitella, P.: Modifications in blood and spinal fluid lactic and pyruvic acid before and after electroshock. *Boll. Soc. ital. biol. sper.* 26:1219, 1950.
- ³⁷ De Toni, G.: Streptomycin in tuberculous meningitis and in miliary tuberculosis: Results in 235 cases at Clinica Pediatrica de Genoa. *Athena.* 16:207, 1950.
- ³⁸ Dietz, A. A., Schmerl, E., and Steinberg, B.: Chemistry of pituitary principles acting upon ocular tension. *Am. J. Ophth.* 33:1349, 1950.
- ³⁹ Donovan, A. M., Foley, J. M., and Moloney, W. C.: The precipitation of CSF globulin by zinc sulfate. *J. Lab. & Clin. Med.* 37:374, 1951.
- ⁴⁰ —: The precipitation of CSF by zinc sulfate. *J. Nerv. & Ment. Dis.* 114:82, 1951.
- ⁴¹ Dripps, R. D. and Vandam, L. D.: Hazards of lumbar puncture. *J.A.M.A.* 147:1118, 1951.
- ⁴² Dwyer, C. S.: Immediate untoward reactions to spinal anesthesia. *Am. J. Surg.* 81:172, 1951.
- ⁴³ Eastham, M. D. and Keay, K. R.: The carbohydrates of human cerebrospinal fluid. *Biochem. J.* 50:iv, 1951.
- ⁴⁴ Effron, A. S. and Perry, G.: Grave spinal cord paralysis caused by spinal anesthesia. *Surg., Gynec. & Obst.* 91:385, 1950.
- ⁴⁵ Escarza, J. F.: A practical method for determining small amounts of glucose in body fluids, blood, or CSF. *Rev. asoc. bioquim., Argentina.* 10:36, 1944.
- ⁴⁶ Fisk, A. A., Chanutin, A., and Klingman, W. O.: Observations on a rapidly migrating electrophoretic component of cerebrospinal fluid. *Proc. Soc. Exper. Biol. & Med.* 78:1, 1951.
- ⁴⁷ Fletcher, A. P.: Intrathecal tuberculin in tuberculous meningitis. *Lancet.* 261:290, 1951.
- ⁴⁸ Franco, V. and Klein, B.: A microdetermination of chlorides in serum and spinal fluid. *J. Lab. & Clin. Med.* 37:950, 1951.
- ⁴⁹ Glesne, O. G.: Lumbar puncture headaches. *Anesthesiology.* 11:707, 1950.
- ⁵⁰ Gloz, H. C.: The influence of ultrashort waves on the cerebrospinal fluid and on the vessels of the retina. *Strahlentherapie.* 80:535, 1949.
- ⁵¹ Goldensohn, E. S., Whitehead, W., Parry, T. M., Spencer, J. N., Grover, R. F., and Draper, W. B.: Diffusion respiration IX. Effect of diffusion respiration and high concentration of carbon dioxide on CSF pressure of anesthetized dogs. *Am. J. Physiol.* 165:334, 1951.
- ⁵² Goodall, A. L.: External rectus paralysis: an unusual complication of spinal puncture. *Glasgow M. J.* 31:417, 1950.
- ⁵³ Gross, B. A.: Quantitative spinal fluid protein determination. A comparative study. *Am. J. Syph., Gonorr. & Ven. Dis.* 35:350, 1951.
- ⁵⁴ Hart, J. R. and Whitacre, R. J.: Pencil-point needle in prevention of postspinal headache. *J.A.M.A.* 147:658, 1951.
- ⁵⁵ Heepe, F., Helmuth, K., and Lambrecht, E.: Test for the total proteins in the

- cerebrospinal fluid using photoelectric determinations of the opalescence caused by sulfosalicylic acid, trichloroacetic acid, and potassium ferrocyanide-acetic acid. *Ztschr f. Kinderh.* 69:331, 1951.
- ⁵⁶ Helrich, M., Papper, E. M., Bordie, B. B., et al.: Fate of intrathecal procaine and spinal fluid level required for surgical anesthesia. *J. Pharmacol & Exper. Therap.* 100:78, 1950.
 - ⁵⁷ Homma, Y.: Suboccipital spinal puncture needle devised by Daito and Homma. *Otolaryng. Nippon Igaku Zasshi K. K.* 22:18, 1950.
 - ⁵⁸ Homolka, J. and Krupicka, V. Z.: Polarography of the CSF. *Časop. lék. Česk.* 89:344, 1950.
 - ⁵⁹ Horwath, V. S.: Barbiturate idiosyncrasy following lumbar puncture. Case report. *M. J. Australia.* 2:622, 1950.
 - ⁶⁰ Hüllinghorst, R. L., Burns, K. F., Young Tai Choi, and Whatley, L. R.: The epidemic of 1949. Japanese B encephalitis in Korea. *J.A.M.A.* 145:460, 1951.
 - ⁶¹ Ingerslev, H.: The clinical importance of the hydrochloric acid-collargol reaction. *Nord. med.* 42:1895, 1949.
 - ⁶² Janbon, N., Bertrand, L., and Izarn, P.: Increased fat content of the CSF in a case of optic neuromyelitis. *Rev. neurol.* 81:740, 1949.
 - ⁶³ Kabat, E. A., Wolf, A., Bezer, A. E., and Murray, J. P.: Studies on acute disseminated encephalomyelitis produced experimentally in rhesus monkeys: VI. Changes in the CSF protein. *J. Exper. Med.* 93:615, 1951.
 - ⁶⁴ Kang, H. J. and Kao, T. C.: The electrolytic method for the detection of tubercle bacilli in CSF. *Chinese M. J.* 66:560, 1948.
 - ⁶⁵ Kaplan, L. and Kennedy, F.: The effect of head posture on the manometrics of the cerebrospinal fluid in cervical lesions: A new diagnostic test. *Brain.* 73:337, 1950.
 - ⁶⁶ Kemali, D.: Cromatografia degli aminoacidi liberi nel liquido cefalorachidiano. *Acta neurol.* 6:312, 1951.
 - ⁶⁷ — and Avio, C. M.: Presence and determination of acetic acid in the CSF. *Acta neurol. Napoli.* 5:671, 1950.
 - ⁶⁸ Kent, J. F. and Neurath, H.: Studies in complement fixation. II. Establishment of optimal concentrations of serum and CSF for diagnosis. *Federation Proc.* 10:12, 1951.
 - ⁶⁹ Kerr, W. J., Jr. and Shaw, E. B.: Diagnosis and treatment of meningitis. *California Med.* 73:325, 1950.
 - ⁷⁰ King, E. J.: Estimation of protein in urine and CSF with permanent turbidimetric standards of perspex. *Biochem. J.* 48:50, 1951.
 - ⁷¹ Kiss, F.: Reabsorption of CSF and the arachnoid vessels. *Magy. Sebészet, Budapest.* 3:73, 1950.
 - ⁷² Koch, R. A.: Value of divided CSF specimens. *J. Ven. Dis. Inform.* 31:251, 1950.
 - ⁷³ Kodama, T., Kanno, S., Muto, N., Kawamura, T., and Hoshino, S.: Colorimetric determination of acetone bodies in the cerebrospinal fluid. *Igaku to Seibutsugaku (Med. & Bio.).* 19:1, 1951.
 - ⁷⁴ Koenigstein, H.: Shifting of cations in the cerebrospinal fluid as a cause of pruritis. *J. Invest. Dermat.* 17:99, 1951.
 - ⁷⁵ Kornushenko, N. P., Kaganova, S. S., and Berezantcheva, L. F.: Effect of streptomycin on M. tuberculosis in the cerebrospinal fluid. *Probl. Tuberk.* 2:58, 1950.
 - ⁷⁶ Kubik, C. S., Perlo, V. P., and Goodall, E. B.: The change in eyegrounds and CSF in hypertension. *J. Nerv. & Ment. Dis.* 114:79, 1951.
 - ⁷⁷ Labhart, H., Schweizer, W., and Staub, H.: Mikroelektrophoretische Untersu-

- chung von normalem und pathologischem Liquor cerebrospinalis. *Confinia neurol.* 11:325, 1951.
- ⁷⁸ Larson, D. L.: Bacterial capsular polysaccharides in the CSF on patients with purulent meningitis. *J. Clin. Investigation* 30:582, 1951.
- ⁷⁹ Lehman, H. E. and Kral, V. A.: Studies on iron content of CSF in different psychotic conditions. *Arch. Neurol. & Psychiat.* 65:326, 1951.
- ⁸⁰ Lembcke, W.: Concerning diminished intracranial pressure. *Ztschr. ärztl. Fortbild.* 44:645, 1950.
- ⁸¹ Leusen, I.: Effects of the composition of the CSF on the central nervous system. *Bruxelles-méd.* 30:2339, 1950.
- ⁸² —: Influence of the CSF pH on respiration. *Arch. internat. physiol.* 57:432, 1950.
- ⁸³ —: Influence of the cerebrospinal fluid pH on blood pH. *Arch. internat. physiol.* 58:112, 1950.
- ⁸⁴ —: Blood and cerebrospinal fluid pH and respiratory function. *Arch. internat. physiol.* 58:115, 1950.
- ⁸⁵ Levinson, A., Luhan, J. A., Mavrelis, W. P., and Herzon, H.: Effect of streptomycin on tuberculous meningitis. Pathologic study. *J. Neuropath. & Exper. Neurol.* 9:406, 1950.
- ⁸⁶ Lickint, F.: The urea nitrogen content of the cerebrospinal fluid. *Arch. f. Psychiat.* 186:194, 1951.
- ⁸⁷ —: The residual nitrogen of cerebrospinal fluid (with particular attention to its relation to other nitrogen-containing constituents). *Arch. f. Psychiat.* 186:198, 1951.
- ⁸⁸ Linck, K.: Human blood, urine, and spinal fluid alcohol levels in acute intoxication and their relation to the time of death. *Deutsche Ztschr. ges. gerichtl. Med.* 39:514, 1949.
- ⁸⁹ Longo, V. and Uccheddu, G. M.: Hyperextension of the head: a new technique for exploration of the spinal subarachnoid spaces. *Acta. Neurol. Napoli.* 5:402, 1950.
- ⁹⁰ Lorber, J.: Studies of the CSF circulation in tuberculous meningitis in children. *Arch. Dis. Childhood* 25:404, 1950.
- ⁹¹ —: Studies of CSF circulation in tuberculous meningitis in children: II. Review of 100 pneumoencephalograms. *Arch. Dis. Childhood.* 26:28, 1951.
- ⁹² Lotmar, F.: Changes in the cerebrospinal fluid in multiple sclerosis. *Schweiz. Arch. Neurol. & Psychiat.* 66:193, 1950.
- ⁹³ Lush, B., Crowley, M. F., Fletcher, E., and Buchan, J. F.: Total and differential protein levels in the blood and cerebrospinal fluid in rheumatoid arthritis. *Ann. Rheumat. Dis.* 10:153, 1951.
- ⁹⁴ McCrumb, F. R., Hall, H. E., Imburg, J., Merideth, A., Helmhold, R., Basora y Defilo, J., and Woodward, T. E.: Treatment of *Hemophilus influenzae* meningitis with chloramphenicol and other antibiotics. *J.A.M.A.* 145:469, 1951.
- ⁹⁵ McDaniel, T. W., Jr. and Talbot, D. R.: Electroencephalographic findings in near lethal phenobarbital poisoning associated with increased spinal fluid protein. *Am. EEG Soc.* 5:21, 1951.
- ⁹⁶ Mendelsberg, S. B.: Fulminating mumps meningoencephalitis with recovery. *J. Pediat.* 39:87, 1951.
- ⁹⁷ Müller, R.: Correlation between state of CSF and clinical picture in disseminated sclerosis. *Acta med. scandinav.* 139:153, 1951.
- ⁹⁸ Münch-Petersen, S.: The copper content in CSF in adults (and children) with and

- without central nervous system disorders. *Acta Psychiat. et Neurol.* 25:251, 1950.
- ⁹⁹ Neel, A. V.: The content of cells and protein in the cerebrospinal fluid. *Acta psychiat.* 25:275, 1950.
- ¹⁰⁰ Neill, J. M., Sugg, J. Y., and McCauley, D. W.: Serologically reactive material in spinal fluid, blood and urine from a human case of cryptococcosis. (torulosis). *Proc. Soc. Exper. Biol. & Med.* 77:775, 1951.
- ¹⁰¹ Nicholls, E. E.: Incidence of normal spinal fluid in acute poliomyelitis. *J. Pediat.* 37:894, 1950.
- ¹⁰² Nichols, E.: Meningo-encephalitis due to brucellosis with report of case in which *B. abortus* was recovered from cerebrospinal fluid, and review of literature. *J.A.M.A.* 148:73, 1952.
- ¹⁰³ Otto, E.: CSF fistulas and pneumatocele in cranial lesions. *Chirurgia.* 21:565, 1950.
- ¹⁰⁴ Poggiali, A.: Lysozyme activity of cerebrospinal fluid (CSF). *Riv. di pat. nerv.* 72:299, 1951.
- ¹⁰⁵ Praetorius, E.: An enzymic method for the determination of uric acid by ultraviolet spectrophotometry. *Scandinav. J. Clin. & Lab. Invest.* 1: 222, 1949.
- ¹⁰⁶ Preziosa, I.: The Weltman test in the blood and CSF of schizophrenics. *Annali, Bisceglie.* 2:181, 1950.
- ¹⁰⁷ Rabe, E. F. and Curnen, E. C.: Occurrence of lysozyme in CSF and serum of infants and children. *J. Pediat.* 38:147, 1951.
- ¹⁰⁸ Rabiner, A. M.: Concerning neurologic complications following spinal anesthesia. *New York State J. Med.* 50:2546, 1950.
- ¹⁰⁹ Rausch, L. and Graul, E. H.: Stabilization of sugar content of CSF samples by addition of sodium fluoride. *Med. Klin.* 45:667, 1950.
- ¹¹⁰ Redfearn, J. W. T., Elithorn, A., Till, K., and Ibbott, F. A.: Penicillin in the CSF. *Lancet.* 257:652, 1949.
- ¹¹¹ Reimers, C. and Neudeck, J.: Disturbances of CSF equilibrium after closed cerebral trauma and the effect of cervical sympathetic block thereon. *Deutsche Ztschr. Nervenhe.* 164:509, 1950.
- ¹¹² Rice, G. G. and Dabbs, C. H.: The use of peridural and subarachnoid injections of saline solution in the treatment of severe postspinal headache. *Anesthesiology.* 11:17, 1950.
- ¹¹³ Saifer, A.: Estimation of increased gamma globulin and fibrinogen in cerebrospinal fluid. A serial dilution-flocculation method. *J. Lab. & Clin. Med.* 36:130, 1950.
- ¹¹⁴ Schneider, G. and Wallenius, G.: Electrophoretic studies on cerebrospinal fluid proteins. *Scandinav. J. Clin. & Lab. Invest.* 3:145, 1951.
- ¹¹⁵ Sedallian, P., Maral, R., Exbrayat, C., et al.: Symptomatologic value of sugar content of cerebrospinal fluid in course of tuberculous meningitis in adults. *J. de méd. de Lyon.* 32:755, 1951.
- ¹¹⁶ —, Maral, R., Traeger, J., and Aventurier, G.: Permeability of the meninges in the course of meningitis, especially the tuberculous form. *J. de méd. de Lyon.* 31:673, 1950.
- ¹¹⁷ Séguin, F.: Ultraviolet spectrophotometric studies on CSF in normal and psychotic individuals. *Canad.M.A.J.* 64:51, 1951.
- ¹¹⁸ Sophian, L. H. and Connolly, V. J.: Ultraviolet absorption spectra of normal CSF. *J. Physical & Colloid Chem.* 55:712, 1951.
- ¹¹⁹ Spiegel-Adolf, M. and Wycis, H. T.: Ultraspectrophotometry of cerebrospinal fluids in tumors of the central nervous system. *Confinia neurol.* 11:87, 1951.

- ¹²⁰ —, Wycis, H. T., and Spiegel, E. A.: Chemical analysis of spectrophotometric findings in the CSF. *J. Nerv. & Ment. Dis.* 113:529, 1951.
- ¹²¹ Stefanini, M. and Schergna, E.: Phlogogenic substances in the cerebrospinal fluid (with special regard to nervous diseases of probable allergic pathogenesis). *Rev. crit. Clin. Med.* 50:108, 1950.
- ¹²² Tortolini, E.: The glucose content of the CSF in diabetic patients. *Policlinico (sez. prat.)* 54:805, 1947.
- ¹²³ Trautman, S. and Ambard, L.: Chlorides in spinal fluid in normal and pathological conditions. *Bull. Acad. nat. Méd.* 135:105, 1951.
- ¹²⁴ Urban, N. and Stechern, A.: Gravimetric determination of sodium in blood serum and CSF. *Biochem. Ztschr.* 321:388, 1951.
- ¹²⁵ Von Storch, T. J. C., Lawyer, T., Jr., and Harris, A. H.: Colloidal gold reaction in multiple sclerosis. *Arch. Neurol. & Psychiat.* 64:668, 1950.
- ¹²⁶ White, D. N. and Fyles, S.: Cerebrospinal fluid manometry. *Canad. M.A.J.* 62:384, 1950.
- ¹²⁷ Whitlock, C. M. Jr., Hunt, A. D. Jr., and Tashman, S. G.: A single, simple, turbidimetric method for the assay of aureomycin, chloramphenicol, penicillin, streptomycin, and terramycin in capillary blood and other body fluids. *J. Lab. & Clin. Med.* 37:155, 1951.
- ¹²⁸ Williams, A. L.: Pathology of tuberculous meningitis, with particular reference to modification in pathology following treatment with streptomycin. *M. J. Australia.* 38:680, 1951.
- ¹²⁹ Wilson, H. M. and Duryea, A. W.: Cryptococcus meningitis (torulosis) treated with a new antibiotic, actidione. *Arch. Neurol. & Psychiat.* 66:470, 1951.
- ¹³⁰ Wright, R. D., Thayer, J. D., Nicholson, F. P., and Arnold, R. C.: Penicillin levels in spinal fluid after intramuscular injection of procaine penicillin. *J. Ven. Dis. Inform.* 32:39, 1951.
- ¹³¹ Yano, M.: The mercuric iodide reaction as applied to the cerebrospinal fluid. *Igaku to Seibutsugaku. (Med. & Biol.)* 19:247, 1951.
- ¹³² Zubrod, G.: Experimental Klebsiella meningitis treated with intrathecal and intramuscular streptomycin. *Bull. Johns Hopkins Hosp.* 84:461, 1949.

Radiology of the Skull and Central Nervous System

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SKULL

ROUNDED defects in the midline of the cranium may be on the basis of congenital dermal sinuses or dermoid cysts. These defects are single and vary in size from two mm. to three cm. The dermal sinuses extend into the brain and may end in cysts, either in the epidural, subdural, or sub-arachnoid spaces, but more often extend into the brain tissue. Matson and Ingraham²⁸ report ten cases with intracranial extension of a congenital dermal sinus. Five of these terminated in a cerebellar cyst and two extended into the ventricular area. The remainder terminated in the meninges.

Fibrous dysplasia of the skull may simulate meningioma according to Feiring, Feiring and Davidoff.¹⁵ In three of their five cases, the roentgen appearance was identical, and, therefore, exploration was necessary. Body section radiography in the coronal and sagittal planes is recommended in the diagnosis of anomalies of the cranio-vertebral junction including platybasia and other types of basilar impression. Confusing shadows are eliminated and important landmarks are easily identified on planigrams. The authors, Gvozdanovic and Dogan,¹⁹ discuss the diagnostic criteria and features of basilar impression. Practically all cases of cleido-cranial dysostosis have one or more other anomalies according to Cole and Levin⁷ who review the subject and present three cases.

In a series of 84 cases of cerebrospinal rhinorrhea studied by Lewin and Cairns,³⁰ 11 were found to have a tear of the dura over the sphenoid sinus, secondary to a fracture. When a fracture in this region is suspected, a careful search should be made for air, particularly in the region of the cisterna chiasmatis, because its presence allows an unqualified diagnosis of traumatic pneumocephalus.

The radiographic findings in Sturge-Weber's syndrome are detailed in an article by DiChiro and Lindgren,⁹ who report 14 cases, 10 of which were proven by pathologic studies. The remaining four presented characteristic findings, including characteristic calcification in the brain, port wine nevus, glaucoma and convulsive seizures. Conventional radiographs reveal asymmetry of the skull with underdevelopment corresponding to the underlying

cerebral disease. Asymmetry is best demonstrated by the occipital view. The authors used encephalography and angiography in the diagnostic regime and report both characteristic and less typical findings.

Multiple curvilinear calcifications in the cerebral hemispheres, typical of toxoplasmosis, were found in six patients with this disease by Sutton.⁴⁸ The author believes the only similar calcifications occur in Torulosis. The lungs should be examined radiographically in patients with acute bulbar poliomyelitis, because of the high incidence of pulmonary complications.²³

Less than 60 per cent of craniopharyngiomas show calcification in the opinion of Lindgren and DiChiro,³⁵ who report 54 of their own cases, and 238 from the literature. In 87 per cent of the cases, the sella was abnormal on the basis of pressure. Pneumography is of considerable help in differentiating this tumor from gliomas. It is sometimes impossible to differentiate a chromophobe adenoma from an intrasellar craniopharyngioma. Fortunately, a high percentage of the latter tumors are extrasellar. The sella turcica is a sensitive barometer of conditions within the cranial cavity. Epstein and Davidoff¹³ studied 50 patients with tumors either in or near the sella turcica that produced pronounced sellar changes. Of these, 28 were pituitary adenomas, 6 craniopharyngiomas, 4 aneurysms of the internal carotid artery, and 5 malignant tumors originating in the nasopharynx or sinuses. Six were metastatic from distant sites and one arose in the frontal fossa and invaded the sella. Other causes of sellar erosion are listed. Pneumoencephalographic examination is of great importance in the differential diagnosis. In another article dealing with changes in the dorsum sellae, Epstein¹² emphasizes the necessity of a careful study of the posterior wall in the roentgen diagnosis of intracranial disease. He particularly stresses a well known fact, namely, any disease that produces enlargement of the third ventricle is apt to cause erosion of the dorsum sellae. Extension of three pituitary chromophobe tumors into the nasal cavity is reported and discussed by Kay, Lees and Stout.²⁵

The roentgen manifestations of 183 patients with proved cerebellopontine angle tumors are reported by Hodes, Pendergrass and Dennis.²¹ Their series includes 134 eighth nerve tumors, 19 meningiomas, 16 gliomas, 7 cholesteatomas and 7 assorted lesions. They found localizing roentgen evidence of acoustic nerve tumors in 85 per cent of the patients included in the report. About half of the patients with cerebellopontine angle meningiomas revealed roentgen changes of localizing value. Three of the patients with cerebellopontine angle cholesteatomas showed erosion of the internal auditory canal. Only one patient of 16 with a glioma showed radiographic abnormalities. In about half of the patients with eighth nerve tumors, the hypophyseal fossa was enlarged. In about 60 per cent, early atrophy to frank destruction of the dorsum sellae was noted. The authors emphasize

the necessity of familiarity with the normal variations of the petrosal pyramids and internal acoustic meati, in order to avoid misinterpreting variations as positive findings. Occasionally, angle tumors can be identified only by pneumography, and, therefore, this procedure should be utilized.

Ninety-five per cent accuracy in both the positive and negative diagnosis of intracranial lesions is reported by Ashkenazy, Davis and Martin,² who used a radioactive dye, di-iodofluorescein in the diagnosis and localization of intracranial tumors. The affinity for dye is related to the vascular pattern and proportional to the cellularity. The highest concentrations were found in metastatic lesions and the lowest in cystic lesions. Subdural hematomas do not concentrate the dye. Moore and co-workers³⁹ state that certain tumors such as acoustic neuromas and pituitary tumors do not take up sufficient dye for detection.

ANGIOGRAPHY

The embryologic basis of intracranial vascular anomalies demonstrable by angiography is reviewed by Sugar,⁴⁷ and affords a better understanding of angiographic pathology. Aneurysms usually occur at the sites of developmental vascular anastomoses, often as a dilatation of the remnant of an embryonic vessel. Dilation of vascular channels that usually obliterate give rise to telangiectases and arterio-venous malformations. Automatic roentgen equipment capable of making simultaneous antero-posterior and lateral exposures at the rate of 2 per second is described by Scott and Seaman.⁴⁵ Roll film is used in Fairchild cameras so that complete vascular filling in all phases can be observed with a single injection. This reduces the hazard and permits a more complete study of the intracranial vessels. This is of particular value in vascular anomalies. However, in the opinion of many radiologists, the detail of films exposed in this manner is deficient and tumor "staining" may not be demonstrable.

Thorotrast as an angiographic medium should be condemned according to Thomas, Henry and Kaplan,⁵¹ due to the high incidence of hepatic and splenic fibrosis following its use. They convassed 68 radiologists and found that in 4325 cases, only five later developed malignant neoplastic disease, a number deemed insignificant. Bloor et al.^{3, 4} found that all contrast media produced severe abnormalities in cerebral electroactivity and vascular permeability varying directly with the amount, concentration, and time interval between injections. Smith and associates⁴⁶ found a variation in toxicity between batches, suggesting that chemical impurities may be a factor. Dunsmore, Scoville and Whitcomb¹⁰ had 14 major complications in 147 angiograms in 108 patients, including 3 deaths and 4 permanent paralyses. The serious cases were those in whom a secondary thrombosis and infarction developed. It is felt by the authors that angiography should

not be employed in the older age group and that papaverine should be administered preoperatively in all cases. Idbohrn²² reports an interesting complication of percutaneous angiography. Intramural dye injection was followed by an intramural hematoma with demonstrable reduction of the carotid lumen.

The percutaneous method of carotid angiography has led to more common utilization of angiography. Koppang²⁶ reports that at his institution in Norway, angiographic examinations increased from 114 in 1945 to 614 in 1949. One operator in the latter year was successful in 354 of 359 attempts. The common carotid artery is punctured rather than the internal carotid. The opposite carotid is compressed routinely at the time of injection and frequently filling of both sides of the cerebral circulation is obtained.

Spasm of the larger intracranial arteries was demonstrated by comparative angiograms in 12 instances in 400 arteriograms by Ecker and Riemen-schneider.¹¹ Seven occurred in saccular arterial aneurysms at or near the circle of Willis. This is believed by the authors to be a protective phenomenon secondary to traction on the vessel wall. Others feel that it may be related to trauma to the vessel wall in inserting the needle. It does produce a delay in circulation time and is as reported a source of error in interpretation.

The value of angiography in the diagnosis of traumatic intracranial hemorrhage has been re-emphasized by Webster et al.⁵² who review their experience in a group of 30 seriously ill patients. The differentiation of intracerebral and extracerebral hematoma or their concurrence can be achieved with accuracy and safety far superior to the exploratory trephine. Two cases of bleeding aneurysm were discovered, clinically simulating post-traumatic intracranial hemorrhage.

The neurologic syndrome produced by thrombosis of the internal and common carotid arteries may simulate tumor, and, therefore, its recognition through angiography is essential. Johnson and Walker²⁴ review 101 cases from the literature and submit six of their own. The majority involve only the internal carotid artery. The condition may be suspected when contralateral filling is obtained in angiography, but for accurate diagnosis, the vessel must be visualized in the neck. The obstruction usually is at the carotid bifurcation and next most commonly at the syphon. Pneumographically, the homolateral ventricle is dilated.

Vertebral angiography has provoked considerable comment in the literature, particularly with reference to the percutaneous technic.^{33, 49} This is successful in two-thirds of the cases. Care must be exercised to avoid the injection of the subarachnoid space and extravasation. A much more effective and safer method is introduced by Radner,⁴¹ who passed a ureteral

catheter from the radial artery directly into the vertebral, with only one failure in 239 catheterizations. All authors agree that the high incidence of variation in the vertebral system makes diagnosis by vascular displacement impossible. Occasionally, pathologic neoplastic vessels are demonstrable, but the method is mainly employed to diagnose vascular pathology such as aneurysms and malformations. Pneumography is preferred for neoplastic localization in this area.

The efficacy of treatment of avascular cerebral lesions by carotid-jugular anastomosis can be improved according to Hammer and co-authors,²⁰ by eliminating the 80 per cent of cases in whom large intracranial vascular shunts exist, as determined by retrograde injection of the internal jugular vein. The shunts are contra-indications to creation of an arterio-venous fistula, which may produce serious complications as well as negate the attempt to increase blood supply. Tarlov and associates⁶⁰ report three such cases studied angiographically postoperatively. Proptosis in one required obliteration of the anastomosis.

Dural sinus venography by direct injection of the sagittal sinus or retrograde injection from the jugular bulb through a catheter inserted from the arm has been of great value according to Ray, Dunbar and Dotter,⁴² and is far more satisfactory than venograms obtained following arteriography. Direct neoplastic extension into the sagittal sinus is demonstrable and of aid to the surgeon. The syndrome called variously pseudotumor cerebri, serous meningitis or otitic hydrocephalus has been clarified and attributed to venous obstruction. In four instances of this condition, three had obstruction to the posterior third of the superior sagittal sinus and one a post-mastoiditis occlusion of the ipsilateral transverse sinus, the opposite side being congenitally small. Scott⁴⁴ employs the direct injection technic and considers the method valuable.

PNEUMOGRAPHY

The hazardous and traumatic nature of ventriculography is emphasized by Falk,¹⁴ who found calcification intracranially at the site of ventricular puncture in 13 per cent of 203 patients re-examined one month to several years postoperatively. Four per cent had calcification in the needle tracks and nine per cent immediately beneath the burr hole. The author recommends that encephalography be employed whenever possible in lieu of ventriculography. Casamajor, Laidlaw and Kozinn⁶ re-emphasize that oxygen encephalography produces symptoms which are less severe and of shorter duration than air encephalography. The severity and duration of symptoms are directly proportional to the amount of gas employed. Pre-operative morphine administration has been abandoned because of vomiting and respiratory complications.

Facts and fallacies in the pneumographic diagnosis of cortical atrophy are very well discussed and illustrated by Lindgren.³⁴ The need for better knowledge of normal variations and for objective diagnosis is stressed. Atrophic lesions may be cortical or central and localized or generalized. The last results in change in size and shape of all or portions of the ventricular system. The cisternae and sulci may be dilated or obliterated. A similar pneumographic appearance is seen in different pathologic process, and, therefore, is not characteristic. Zaunbauer⁵³ reports a cyst of the septum pellucidum in a patient with a gunshot wound of the head. After relief of symptoms, a repetition of the encephalogram revealed that the septum pellucidum had returned to normal. The author suggests that at least a few of the cases reported as closed cysts might be post-inflammatory in nature and transitory.

SPINE

Diastematomyelia associated with a spina bifida of the cervicodorsal area in a twelve-year-old boy is reported by Cowie.⁸ A bony spicule passed from the vertebral body to an irregularly fused lamina and it divided the spinal canal into two dural sacs. There was an associated duro-dermal sinus that extended into one of the sacs.

In order to clearly demonstrate the fifth lumbar intervertebral foramina, it is necessary to rotate the patient 60 degrees from the supine and angle the tube 25 to 30 degrees towards the patient's feet, according to Kovacs.²⁷ He believes cartilaginous protrusions as well as osteophytes are more clearly and frequently demonstrated by this method than by the usual technic. In better than 80 per cent of 65 patients with sciatica, the author was able to demonstrate either an osteophyte or a cartilage protrusion. In only one of this group was it possible to show changes on routine film examination. Operative confirmation was obtained in 23 instances. This method of examination with slight modification is substantiated by Kröker,²⁸ who was able to demonstrate dorsal or dorsolateral osteophytes indicative of long-standing herniated discs in 71 per cent of 164 patients. In this group, 102 had spurs and 15 had prolapsed discs. Kröker used an angulation of 15 degrees towards the feet and rotated the patient 60 degrees from the supine.

The incidence of disc rupture increases in anatomic studies from 20 per cent at age 20 to over 50 per cent at age 45. Lindblom³² believes that with a few exceptions, low back and sciatic pain are on the basis of disc rupture and protrusion. The author made a comprehensive study of the gross and histologic nature of the intervertebral disc and evaluated back-ache in its relation to rupture of the disc. Reverse spondylolisthesis at the lumbosacral junction was noted in 16 per cent of 493 lumbosacral disc protrusions. Gillespie¹⁷ believes backsliding of the fifth lumbar vertebra

is often associated with disc disease, and, therefore, an important finding in the diagnosis of disc protrusion.

Cysts in the spinal canal occur around the nerves in the epidural, subdural and subarachnoid spaces. They are sometimes post-traumatic or postoperative in origin and simulate the pain of ruptured intervertebral discs. Schreiber and Haddad⁴³ found erosion of the sacrum due to a subarachnoid cyst in two patients and noted a complete block of the subarachnoid space as determined by myelography in another. These lesions are often overlooked, and, therefore, should always be considered when pain is not on the basis of a disc protrusion or a tumor.

Lindblom³¹ studied five living subjects and three anatomic specimens of so-called persistent epiphysis or persisting limbus vertebrae by discography, and thereby discovered anterior transosseous protrusion of the intervertebral disc. A fissure between the separated fragment and the body communicated with the disc. This work confirms that of Schmorl and Jungmanns. The limbus may be anterior or posterior.

Acute osteochondritis of the spine was seen by Günsel¹⁸ in three male patients following lumbar sympathectomy for endarteritis obliterans apparently due to interference with the blood supply to the spine. Changes are first seen in the intervertebral discs and then in the subchondral areas. The disease is segmental, proceeding to all vertebrae in the area involved.

Anderson¹ studied the cranial and vertebral venous systems by the injection of diodrast into the dorsal vein of the penis in 22 patients. Raising the intra-abdominal or intrathoracic pressure causes the dye to go into the cranio-vertebral venous system by temporarily blocking the usual channels. Batson's work on the vertebral veins indicating their importance in the dissemination of metastatic tumor was verified.

Skin testing with Pantopaque to determine sensitivity is contraindicated in the opinion of Luce, Leith and Burrage,³⁷ because intradermal testing in their patients sensitized them and resulted in non-infectious meningitis from small amounts of residual Pantopaque in the subarachnoid space. This effect was noted in only two patients, but all other patients subjected to Pantopaque myelography who were not skin-tested showed no evidence of meningitis. There was an acute flare-up of the skin reaction coincidentally with the development of acute meningitis. The latter condition was transient and complete recovery occurred in both patients.

Abrodil (Skiodan) is recommended for myelography in the lumbar region by Lange and Ødegaard.²⁹ The advantages of this contrast medium are its absorption from the spinal canal and nerve roots in about two hours and its diagnostic value in the visualization of nerve roots and root sleeves. Defective filling of the root sleeve and widening of the root are valuable

diagnostic signs obtained when this material is used. The authors recommend this contrast medium in dealing with herniated lumbar discs. The disadvantages are irritating effects manifested as increased root pain for one or two days, diffuse pain in the lower extremity for the same period of time, and pain of shorter duration in the back and lower extremities. Nausea, headache, vomiting and, rarely, convulsions occur. It is unlikely that the substance will gain widespread use in this country, because of the above-mentioned side effects.

The importance of minor myelographic deformities is stressed by Boulton, Kiernan and Childe⁵ in an excellent article dealing with technic of opaque myelography. They emphasize that minor deformities are difficult or impossible to recognize fluoroscopically and for this reason a series of at least 12 spot films should be made whether or not any abnormality is seen on the screen. Oblique views are essential and often confirm the presence of deformities which otherwise would be doubtful or completely overlooked. They use postero-anterior and oblique views routinely and lateral decubitus views in the diagnosis of tumors. An appreciable number of minor deformities occur at the lumbosacral interspace. Emphasis on a correlation between the clinical and roentgen findings is stressed.

Lindquist³⁶ studied hemangiomas of the vertebral column and states this condition is found in 10 to 12 per cent of autopsy studies. The condition may be asymptomatic, or there may be local symptoms, including pain. A compression fracture with myelopathy may occur, and the prognosis is bad. The author reports an excellent result with x-ray therapy in an 18-year-old boy with cord compression at 9-D. There was marked clinical improvement and ten year follow-up showed no change in the x-ray appearance and no recurrence of symptoms.

ROENTGEN THERAPY

Pendergrass and Phillips⁴⁰ advocate ventriculo-encephalography in planning roentgen therapy for brain tumors. They are certain better results are obtained when the tumor is localized prior to roentgen therapy, because it is possible to use smaller portals and avoid normal brain tissue.

Freid and Davidoff¹⁶ analyze the results of roentgen therapy of primary neoplasms of the brain. In the glioblastoma multiforme group of 30 patients, the type of operation and the amount of postoperative radiation did not seem to effect survival. In the group of 15 patients with cerebral astrocytomas, longer survivals appeared to be associated with larger total doses of radiation. The cerebellar medullo-blastomas showed the best results with roentgen therapy. Spongioblastoma polare is not influenced in the authors' opinion.

REFERENCES

- ¹ Anderson, R.: Diodrast studies of the vertebral and cranial venous systems to show their probable role in cerebral metastases. *J. Neurosurg.* 8:411-422, 1951.
- ² Ashkenazy, M., Davis, L., and Martin, J.: An evaluation of the technic and results of the radioactive di-iodofluorescein test for the localization of intracranial lesions. *J. Neurosurg.* 8:301-314, 1951.
- ³ Bloor, B. M., Wrenn, F. R., and Hayes, G. J.: An experimental method for the evaluation of contrast media used in cerebral angiography. *J. Neurosurg.* 8:435-440, 1951.
- ⁴ Bloor, B. M., Wrenn, F. R., and Margolis, G.: An experimental evaluation of certain contrast media used for cerebral angiography. *J. Neurosurg.* 8:585-594, 1951.
- ⁵ Boulton, G. F., Kiernan, M. K., and Childe, A. E.: The importance of minor myelographic deformities in the diagnosis of posterior protrusion of the lumbar intervertebral disc. *Am. J. Roentgenol.* 66:752-763, 1951.
- ⁶ Casamajor, L., Laidlaw, R. W., and Kozinn, P. J.: The technique of pneumo-encephalography in children: Comparative results with air and oxygen techniques. *J. Pediat.* 38:463-467, 1951.
- ⁷ Cole, W. R. and Levin, S.: Cleidocranial dysostosis. *Brit. J. Radiol.* 24:549-555, 1951.
- ⁸ Cowie, R. N.: Diastematomyelia with vertebral column defects. Observations on its radiologic diagnosis. *Brit. J. Radiol.* 34:156-160, 1951.
- ⁹ DiChiro, G. and Lindgren, E.: Radiographic findings in 14 cases of Sturge-Weber syndrome. *Acta radiol.* 35:387-399, 1951.
- ¹⁰ Dunsmore, R., Scoville, W. B., and Whitcomb, B. B.: Complications of angiography. *J. Neurosurg.* 8:110-118, 1952.
- ¹¹ Ecker, A. and Riemenschneider, P. A.: Arteriographic demonstration of spasm of the intracranial arteries. *J. Neurosurg.* 8:660-667, 1951.
- ¹² Epstein, B. S.: Shortening of the posterior wall of the sella turcica caused by dilatation of the third ventricle or certain suprasellar tumors. *Am. J. Roentgenol.* 65:49-55, 1951.
- ¹³ Epstein, B. S. and Davidoff, L.: Advanced atrophy and enlargement of the sella turcica with destruction of the sphenoid. *Am. J. Roentgenol.* 66:884-893, 1951.
- ¹⁴ Falk, B.: Calcifications in the track of the needle following ventricular puncture. *Acta radiol.* 35:304-308, 1951.
- ¹⁵ Feiring, W., Feiring, E. H., and Davidoff, L. M.: Fibrous dysplasia of the skull. *J. Neurosurg.* 8:377-397, 1951.
- ¹⁶ Freid, J. R. and Davidoff, L. M.: Roentgen therapy of primary neoplasms of the brain. *Radiology.* 57:25-36, 1951.
- ¹⁷ Gillespie, H. W.: Vertebral retroposition (reversed spondylolisthesis). *Brit. J. Radiol.* 24:193-197, 1951.
- ¹⁸ Günsel, E.: Über die Spondylosis Chondromalacia. *Fortschr. Geb. Röntgenstrahlen.* 74:522-525, 1951.
- ¹⁹ Gvozdanovic, V. and Dogan, S.: The use of tomography in diagnosis of basilar impression. *Acta radiol.* 35:124-132, 1951.
- ²⁰ Hammer, J. M., Heersema, H. S., MacGregor, J. R., Dew, R. S., Osius, E. A., and DeGroat, A.: Surgical arteriovenous fistula between right common carotid artery and internal jugular vein. *J. Internat. Coll. Surgeons.* 16:289-308, 1951.
- ²¹ Hodes, P. J., Pendergrass, E. P., and Dennis, J. M.: Cerebellopontine angle tumors: Their roentgen manifestation. *Radiology.* 57:395-406, 1951.

- ²² Idbohrn, H.: A complication of percutaneous carotid angiography. *Acta radiol.* 36:155-161, 1951.
- ²³ Jacobson, G., Cohen, S. R., and Carter, R. A.: Pulmonary complications of acute bulbar polymyelitis. *Radiology.* 57:629-641, 1951.
- ²⁴ Johnson, H. C. and Walker, A. E.: The angiographic diagnosis of spontaneous thrombosis of the internal and common carotid arteries. *J. Neurosurg.* 8:631-659, 1951.
- ²⁵ Kay, S., Lees, J. K., and Stout, A. P.: Pituitary chromophobe tumors of the nasal cavity. *Cancer.* 3:695-704, 1950.
- ²⁶ Koppang, K.: Some examples of the diagnostic value of percutaneous carotid angiography. *Acta radiol.* 35:137-145, 1951.
- ²⁷ Kovacs, A.: X-ray examination of the exit of the lower-most lumbar root. *Radiologic clin.* 19:6-13, 1950.
- ²⁸ Kröcker, P.: Über die Röntgenuntersuchung beim lumbalen Bandscheivenvorfall mit Hilfe der Lumboinguinalen Einstellung von Kovacs. *Fortschr. Geb. Röntgenstrahlen.* 74:512-521, 1951.
- ²⁹ Lange, J. and Ødegaard, H.: Abrodil myelography in herniated disc in the lumbar region. *Radiology.* 57:186-192, 1951.
- ³⁰ Lewin, W. and Cairns, H.: Fractures of the sphenoidal sinus with cerebrospinal rhinorrhea. *Brit. M. J.* 1:1-6, 1951.
- ³¹ Lindblom, K.: Discography of transosseous ruptures of intervertebral discs in the lumbar region. *Acta radiol.* 36:12-16, 1951.
- ³² —: Backache and its relation to rupture of the intervertebral discs. *Radiology.* 57:710-719, 1951.
- ³³ Lindgren, E.: Percutaneous angiography of the vertebral artery. *Acta radiol.* 33:389-404, 1950.
- ³⁴ —: Encephalography in cerebral atrophy. *Acta radiol.* 35:277-292, 1951.
- ³⁵ — and DiChiro, G.: Suprasellar tumors with calcification. *Acta radiol.* 36:173-195, 1951.
- ³⁶ Lindquist, I.: Vertebral hemangioma with compression of the spinal cord. Report of a case treated with roentgen with good clinical results. *Acta radiol.* 35:400-406, 1951.
- ³⁷ Luce, J. C., Leith, W., and Burrage, W. S.: Pantopaque meningitis due to hypersensitivity. *Radiology.* 57:878-881, 1951.
- ³⁸ Matson, D. R. and Ingraham, F. D.: Intracranial complications of congenital dermal sinuses. *Pediatrics.* 8:463-474, 1951.
- ³⁹ Moore, G. E., Caudill, C. M., Marvin, J. F., Aust, J. B., Chou, S. N., and Smith, G. A.: Clinical and experimental studies of intracranial tumors with fluorescein dyes. *Am. J. Roentgenol.* 66:1-8, 1951.
- ⁴⁰ Pendergrass, E. P. and Phillips, J. M.: The value of ventriculoencephalography in planning roentgen therapy for brain tumors. *Am. J. Roentgenol.* 66:603-612, 1951.
- ⁴¹ Radner, S.: Vertebral angiography by catheterization. A new method employed in 221 cases. *Acta radiol. Supply.* 87:1-131, 1951.
- ⁴² Ray, B. S., Dunbar, H. S., and Dotter, C. T.: Dural sinus venography. *Radiology.* 58:477-486, 1951.
- ⁴³ Schreiber, F. and Haddad, B.: Lumbar and sacral cysts causing pain. *J. Neurosurg.* 8:504-509, 1951.
- ⁴⁴ Scott, M.: Dural venous sinography. *Am. J. Roentgenol.* 65:619-620, 1951.

- ⁴⁵ Scott, W. G. and Seaman, W. B.: Developments in cerebral angiography with rapid serialized x-ray exposures on roll film 9½ inches wide. *Radiology*. 56:15-30, 1951.
- ⁴⁶ Smith, G. A., Caudill, C. M., Moore, G. E., Peyton, W. T., and French, L. A.: Experimental evaluation of cerebral angiography. *J. Neurosurg.* 8:556-563, 1951.
- ⁴⁷ Sugar, O.: Pathological anatomy and angiography of intracranial vascular anomalies. *J. Neurosurg.* 8:1-22, 1951.
- ⁴⁸ Sutton, D.: Intracranial calcification in toxoplasmosis. *Brit. J. Radiol.* 34:31-37, 1951.
- ⁴⁹ Sutton, D. and Hoare, R. D.: Percutaneous vertebral arteriography. *Brit. J. Radiol.* 24:589-597, 1951.
- ⁵⁰ Tarlov, I. M., Shure, B., Epstein, B. S., Hirsch, E., and Nissen, R.: Brain revascularization after carotid-jugular anastomosis assessed by angiography. *Arch. Neurol. & Psychiat.* 64:847-860, 1950.
- ⁵¹ Thomas, S. F., Henry, G. W., and Kaplan, H. S.: Hepatolienography: Past, present, and future. *Radiology*. 57:669-684, 1951.
- ⁵² Webster, J. E., Dawson, R., and Gurdjian, E. S.: The diagnosis of traumatic intracranial hemorrhage by angiography. *J. Neurosurg.* 8:368-376, 1951.
- ⁵³ Zaunbauer, W.: Über Verbreiterung des Septum Pellucidum. *Fortschr. Geb. Röntgenstrahlen*. 74:549-555, 1951.

III. NEUROSURGERY

CHAPTER 16

Peripheral Nerve Surgery

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THE PAST year has been devoted to a continuing study of data assembled in the post World War II period by both British and American investigators. Recorded experience has been scanty. With one exception, no reports concerning the treatment of casualties of the Korean episode have been reported. King,¹ from the Walter Reed General Hospital, describes an unusual ulnar nerve injury in which all of the intrinsic hand muscles received innervation in part at least from the median nerve. It is of interest that exploration of a rather obvious peripheral nerve injury was delayed from the time of injury on November 12, 1949 until August 1950.

Five papers and one monograph discuss further aspects of World War II surgery. Bowden and Sholl² studied 17 cases of suture and 14 cases of lesion in continuity of the radial nerve in man in whom signs of recovery were manifest in all the muscles normally supplied by that nerve. Using Sunderland's anatomic data, the distances between the suture or lesion and the muscles supplied by the radial nerve were calculated and plotted against the respective times taken for recovery. The pattern of the plotted points again suggested that the rate of advance of functional recovery from muscle to muscle is at first high and then declines. Grantham and Pollard³ have reported the end results in 281 cases of peripheral nerve injury followed from six to 24 months. They report a surprisingly high percentage of what is termed neurologic and functional recovery. The average interval between injury and operation was five months. The criteria for evaluation of neurologic recovery corresponded somewhat to the British system, relating recovery to varying degrees of motor function in proximal and distal muscles and of sensory return in the autonomous zone of the nerve involved. The functional result was qualified as satisfactory or unsatisfactory. The authors stated that recovery in some degree occurred in 90 per cent of cases which

could be sutured successfully. In these, they reported a combined percentage of 59.6 per cent excellent and good results in 116 cases followed from 12 to 24 months. The percentages of satisfactory results in individual nerves corresponded in order with those which have been published previously. Thus, the peroneal nerve showed the lowest percentage recovery, 30.7 per cent, with the musculocutaneous and radial nerves exhibiting percentage recovery returns of 80 and 78 per cent respectively. The enormous complexity of the task of evaluating peripheral nerve regeneration in precise anatomic and functional terms is passed over rather lightly in this contribution.

Tobin⁴ has pointed out again the many advantages that accrue from close cooperation between orthopedic and neurologic surgeon in the control of war injuries of peripheral nerves. This represents a lesson that must be repeated again and again. He recommends the preoperative joint conference method for evaluation of the injury and its therapy and the single operative approach to the combined injury. In his experience, the majority of orthopedic injuries associated with various peripheral nerve lesions were non-unions of compound fracture. This sound clinical discussion closes with a description of standard orthopedic reconstructive procedures that are adaptable to the functional restitution of irreparably damaged peripheral nerves. Seletz has summarized his experience as a military neurosurgeon in two papers and one monograph depicting the operative approaches to peripheral nerve repair. The first⁵ is presented as a miniature atlas containing 17 figures and 51 individual illustrations depicting the surgical anatomy, manifestations of injury and repair of the radial nerve. The illustrative material is superb. The recommendation of a transverse axillary incision for exploration of the lower portion of the brachial plexus would not be acceptable to every neurosurgeon. Seletz presented another series of wash drawings depicting the surgical anatomy of the sciatic nerve⁶ in his second brief atlas. Of particular interest is his recommendation to approach the sciatic nerve from the lateral approach in the mid-thigh where it lies between the long head of the m. biceps femoris and the m. vastus lateralis. (The caption on figure 7, page 300, seems to be in error). The monograph⁷ is again profusely and well illustrated and valuable for its emphasis upon incisional approaches to nerve repair. The surgical anatomy of peripheral nerves is well portrayed. The textual material is scanty and does not contribute much to this otherwise fine contribution.

In the field of civilian-type peripheral nerve injuries, Perret discusses four principles of successful repair.⁸ Early recognition of nerve injury is the most important single factor that will insure a good result after repair. He describes routine methods of diagnosis and then points out the common mistakes in tissue identification that may be made at the time of primary

suture. He advocates primary repair, stating that the sooner the divided nerve ends are sutured, the more successful will be the degree of regeneration. Primary suture is advocated even in a potentially infected wound, under the protection of antibiotics. The third principle of repair has to do with operative technic and routine methods are described. Finally, he advocates autogenous or fresh homogenous grafts for the repair of nerve injuries with extensive nerve gaps, adding, in the face of published evidence to the contrary, that all opportunity to evaluate such fresh homografts was lost in World War II. He rightfully stresses the importance of maintaining the effector mechanism in a functional status during the period of neural regeneration. Phalen⁹ continues his discussion and case presentations of 11 instances of median nerve paralysis developing without any clearcut etiology and involving tissues innervated by the median nerve distal to the wrist. In eight cases, relief was obtained by simple section of the transverse carpal ligament.

Tarlov and his associates¹⁰ report the instance of a patient in whom almost complete sciatic nerve paralysis immediately followed the intragluteal injection of 50,000 Oxford units of penicillin beeswax and peanut oil. Following the observation of this case, animal experiments were carried out with rabbits to ascertain whether or not the neuritis was the result of the action of penicillin itself or of its vehicles. Streptomycin and procaine injections were also studied, as were the effects of hemorrhage in and around the sciatic nerve of rabbits. The experimental observations appeared to show that the paralysis could not have been caused either by rupture or by hemorrhage from the central artery or by the introduction of penicillin alone around or into the epineurium. By their resistance to inflammatory reactions, the epineurium and perineurium seemed to protect the parenchyma of the nerve very effectively. They state that the neuritis was attributable to the introduction of the material directly into the parenchyma of the nerve. The resultant inflammatory reactions were much more intense with the oily than with the soluble penicillin. Streptomycin injections produced similar reactions. After the injection of penicillin into the nerve, in some cases a latent interval varying from eight to seventeen days elapsed before severe impairment of nerve function as manifested by loss of spread reflex in the rabbit occurred. This delayed impairment is the experimental counterpart of the similar delayed onset of symptoms referable to neuritis in human cases in which the neuritis was probably due to progressive inflammatory and fibrotic changes. A warning was noted concerning the site of injection of these materials. Four cases of peripheral nerve injuries have been described by Kolle¹¹ following intramuscular, subcutaneous and paravenous injection of diverse therapeutic substances.

Direct observation of sweating through a 20 plus ophthalmoscope lens

has been advocated by Kahn as a simple adjunct to the diagnosis of primary nerve injury and to the observation of the progress of neural regeneration.¹² A portable electromyograph was described,¹³ designed for clinical and research purposes; future papers will report such studies. Tarlov and his group have continued their search for a suitable substance for neurography¹⁴ and have reported their observations, particularly with pantopaque. This substance produced satisfactory roentgenographic contrast and was much more readily injected than the more viscous lipiodol. Quantities as low as 0.1 cc. to 0.2 cc. produce no functional or histologic abnormality. With larger amounts of pantopaque, degeneration of nerve fibers occurred when the needle penetrated the epineural-perineural barriers. The authors feel that neurography with substances now available has not reached the stage of development where it can be used as a diagnostic method.

Sunderland has continued his fruitful investigations into the effects of denervation upon nerve and muscle fibers and has continued his interest in the neurosurgical problems of repair. In the course of a study on the reaction of peripheral nerve tissue to implanted suture materials (see PROGRESS 1950), Sunderland has further shown that, despite the complete disorganization of the intraneural architecture at the site of implantation, the normal appearance of funiculi and nerve fibers was restored at more distal levels. He gives a word of warning that in peripheral nerve injury cases, or in failed suture-line biopsy material, unfavorable looking tissue may contain axons which are capable of functioning efficiently despite the fact that pathways possessing the characteristic morphologic features of myelinated nerve fibers cannot be detected. This paper represents another contribution to the perplexing clinical problem of neuroma-in-continuity.¹⁵

Sunderland points out that the changes which develop in muscle which has been deprived of its nerve supply are now well known though several details relating to the processes involved remain obscure.¹⁶ It is generally recognized, however, that prolonged denervation often leads to a condition which is incompatible with the restoration of useful function even though the muscle has been satisfactorily reinnervated. An attempt was made in this study to ascertain the extent to which the residual defect after delayed nerve repair is attributable to changes in the nerve itself and how much is due to progressive changes in the denervated muscle. Personal records of a series of fifty-nine patients with peripheral nerve sutures form the basis of this study. Of this group, ten were considered suitable for the study of the capacity of muscles to function efficiently after reinnervation following prolonged periods of denervation. From the study of these patients, it was ascertained that complete or very good restoration of function can occur in reinnervated human muscle after denervation for at least twelve months,

as a result of nerve severance, providing the axons can be directed in sufficient numbers to their original or functionally similar endoneural tubes and end organs, and that the quiescent muscles have been maintained in the best possible condition by appropriate therapy. From this it is concluded that the duration of the denervation and the changes induced in muscle do not assume significance as regards irreversibility within the first twelve months of denervation.

The most potent factors responsible for the residual defect in muscle function after nerve suture are those which lead to a reduction of the number of functionally effective axons which reach the muscle. Such factors are retrograde neuronal degeneration, denervation atrophy of the distal stump, and crossed shunting of regenerating axons.

In the first of two related papers,¹⁷ Sunderland undertook experimental studies to provide details concerning the rate at and the extent to which the distal stump of a severed nerve atrophies. He was interested in the manner in which the process is influenced by variations in the relative amounts of funicular and connective tissue comprising the nerve cross-area. There was noted a progressive decrease in the funicular area as the period of denervation increased. Atrophy proceeded rapidly at first and then more slowly. There was a 40 to 50 per cent reduction at 59 days, a 50 to 60 per cent at 89 days, while at 140 days the residual funicular cross-sectional area was 30 to 40 per cent of its original value. Beyond this point to the 485th day, there was no further change. The extent of atrophy fluctuated irregularly because the funicular-connective tissue ratio has been demonstrated by these observers to be a variable morphological factor. In the second paper,¹⁸ Sunderland observed progressive atrophy of the endoneural tube and showed that by 89 days after denervation, most of the tubes were less than $3\ \mu$ in diameter; at 485 days, no tube larger than $2\ \mu$ was observed. These findings suggest that nerve repair undertaken later than three months after injury must result in permanent immaturity of many of the regenerated fibers and thus a residual disability. His clinical studies of regeneration after delayed nerve repair in humans have indicated that the distal stump retains the capacity of adequately transmitting axons to the periphery for at least 12 months. The implication is obvious that nerve fibers need not be restored to the original diameter for the recovery of muscle function.

Bucker and Meyers¹⁹ have presented another determining factor in peripheral nerve regeneration, showing that the increment of growth which should occur in a given nerve of a rapidly growing animal is abolished during the degeneration and regeneration interval caused by nerve crush. The peripheral stump is, therefore, composed of permanently reduced endoneural tubes which exert a lasting restrictive action on the maturation of medullated fibers. Pollock et al.²⁰ have studied again the effect of electro-

therapy upon retardation of atrophy and acceleration of return of muscle bulk after peripheral nerve injury and repair. Using a variety of unilateral, bilateral, primary and delayed sutures in the cat sciatic nerve, they were not able to find statistically significant differences in treated and untreated muscle. On the other hand, the weight of the denervated and treated gastrocnemius muscle of the rat was uniformly greater than that of the untreated muscle. Histopathologic studies of treated and untreated muscles in the cat showed unpredictable variations.

Gerard²¹ reviews the current physiologic theories concerning pain mechanisms. He demonstrates the concept that causalgic pain may result from simple loss of normal innervation by reference to the development of intense causalgic pain in a phantom limb during spinal anesthesia for an irrelevant condition. Similar cases have been reported by Harrison.²²

Von Hellens²³ describes the results obtained in complete denervation in ten cases of osteoarthritis of the hip, a study somewhat similar to those published in previous issues of *Progress*. Patients were selected in whom pain and limitation of abduction were assumed to be due to adduction contracture. Among six cases with true osteoarthritis the result was excellent or good in five. In the four cases of secondary osteoarthritis, on the other hand, the result was only fair or poor but the preoperative pain at rest disappeared in these cases. The operation is recommended as a relatively safe palliative procedure, especially in the case of old persons with true osteoarthritis in whom the pain is most probably chiefly due to adduction contracture.

Tarlov and his group have again described their efforts to graft the cauda equina of monkeys, using grafts of segments of posterior nerve roots as long as 44 mm. to bridge defects in the anterior roots. Good recovery of nerve-muscle activity was indicated by chronaxie measurements, by stimulation of nerves through skin and by direct stimulation of the repaired nerve roots at reoperation.²⁴ A very mature and intelligent discussion of the problem in man as derived from an intensive study of grafting in the cat has been presented by Hiller.²⁵ Emphasis is rightly placed upon the mesodermal reaction so characteristic of the neuropathology of human grafts. The suggestion is made that experimental studies should be made with embryonic grafts to forestall mesodermal invasion.

Three papers on the effect of ultrasonic energy upon the central and peripheral nervous systems offer another instrument for the study of nerve injury and regeneration. Ultrasonic energy in the amount of 3.0 to 5.8 watts per square centimeter applied to the mid-thigh resulted in complete blocking of, or at least 50 per cent decrease in, the action potential of the intact sciatic nerve in 60 per cent of the dogs studied. The action potential of the dog sciatic nerve was also decreased by direct heating in a manner

strikingly similar to that produced by ultrasonic energy. Histologic changes were variable in the affected sciatic nerves.²⁶⁻²⁸ The matter of ischemic lesions has been freshly reviewed by Richards.²⁹

REFERENCES

- ¹ King, R. B.: Anomalous innervation of the hand muscles. *J. Neurosurg.* 8:528, 1951.
- ² Bowden, R. E. M. and Sholl, D. A.: The advance of functional recovery after radial nerve lesions in man. *Brain.* 73:251, 1950.
- ³ Grantham, E. G. and Pollard, C.: Peripheral nerve surgery, results of 281 cases followed six to twenty-four months. *Ann. Surg.* 134:145, 1951.
- ⁴ Tobin, W. J.: Combined bone and nerve injuries. *Mil. Surgeon,* 109:621, 1951.
- ⁵ Seletz, E.: Injuries of the nervus radialis. An atlas illustrating its normal and surgical anatomy, the motor and sensory manifestations of its injury, and its surgical repair. *Bull. Los Angeles Neurol. Soc.* 16:109, 1951.
- ⁶ —: Injuries of the nervus ischiadicus. An atlas illustrating the normal and pathologic anatomy, diagnosis and surgical repair. *Bull. Los Angeles Neurol. Soc.* 16:292, 1951.
- ⁷ —: Surgery of peripheral nerves. Springfield, Illinois, Charles C Thomas, 1951, p. 212.
- ⁸ Perret, G.: Experimental and clinical investigations of peripheral nerve injuries of the upper extremities. *J.A.M.A.* 146:556, 1951.
- ⁹ Phalen, G. S.: Spontaneous compression of the median nerve at the wrist. *J.A.M.A.* 145:1128, 1951.
- ¹⁰ Tarlov, I. M., Perlmutter, I., and Berman, A. J.: Paralysis caused by penicillin injection: mechanism of complications—a warning. *J. Neuropath & Exper. Neurol.* 10:158, 1951.
- ¹¹ Kolle, K.: Schaden an den peripheren Nerven nach Injektionen. *Deutsche med. Wchnschr.* 76:367, 1951.
- ¹² Kahn, E. A.: Direct observation of sweating in peripheral nerve lesions. Its use as a simple diagnostic test. *Surg., Gynec. & Obst.* 92:22, 1951.
- ¹³ Arieff, A. J., Newman, L. B., and Fizzell, J. A.: 1. A portable electromyograph for clinical and research purposes. *Arch. Phys. Med.* 32:320, 1951.
- ¹⁴ Tarlov, I. M., Berman, D., and Epstein, J.: Experimental neurography. *Am. J. Roentgenol.* 64:974, 1950.
- ¹⁵ Sunderland, S.: The functions of nerve fibers whose structure has been disorganized. *Anat. Rec.* 109:503, 1951.
- ¹⁶ —: Capacity of reinnervated muscles to function efficiently after prolonged denervation. *Arch. Neurol. & Psychiat.* 64: 755, 1950.
- ¹⁷ — and Bradley, K. C.: Denervation atrophy of the distal stump of a severed nerve. *J. Comp. Neurol.* 93: 401, 1950.
- ¹⁸ — and Bradley, K. C.: Endoneural tube shrinkage in the distal segment of a severed nerve. *J. Comp. Neurol.* 93:411, 1950.
- ¹⁹ Buckner, E. D. and Meyers, C. E.: The maturity of peripheral nerves at the time of injury as a factor in nerve regeneration. *Anat. Rec.* 109:723, 1951.
- ²⁰ Pollock, L. J., Arieff, A. J., Sherman, I. C., Schiller, M., Tigay, E., Hiller, F., Liebert, E., and Yacorzynski, S. K.: Electrotherapy in experimentally produced lesions of peripheral nerves. *Arch. Phys. Med.* 32: 377, 1951.
- ²¹ Gerard, R. W.: The physiology of pain: abnormal neuron states in causalgia and related phenomena. *Anesthesiology.* 12: 1, 1951.

- ²² Harrison, G.: "Phantom limb" pain occurring during spinal analgesia. *Anesthesiology*. 6:115, 1951.
- ²³ Von Hellens, A.: Denervation in the treatment of osteoarthritis of the hip joint. *Acta chir. Scandinav.* 102:48, 1951.
- ²⁴ Tarlov, I. M., Berman, S., Kellerman, E., and Moldaver, J.: Cauda equina nerve root regeneration through nerve grafts, an experimental study in monkeys. *J. Neuropath. & Clin. Neurol.* 1: 111, 1951.
- ²⁵ Hiller, F.: Nerve regeneration in grafts. *J. Neuropath. & Clin. Neurol.* 1: 5, 1951.
- ²⁶ Wulff, V. J., Fry, W. J., Tucker, D., Fry, F. J., and Melton, C.: Effects of ultrasonic vibrations on nerve tissue. *Proc. Soc. Exper. Biol. & Med.* 76: 361, 1951.
- ²⁷ Anderson, T. P., Wakins, K. G., Herrick, J. F., Bennett, N. A., and Krusen, F. H.: An experimental study of the effects of ultrasonic energy on the lower part of the spinal cord and peripheral nerves. *Arch. Phys. Med.* 32: 71, 1951.
- ²⁸ Wall, P. D., Fry, W. J., Stephens, R., Tucker, D., and Lettvin, J. Y.: Changes produced in the central nervous system by ultrasound. *Science*. 114: 686, 1951.
- ²⁹ Richards, R. L.: Ischaemic lesions of peripheral nerves: a review. *J. Neurol. Neurosurg. & Psychiat.* 14: 76, 1951.

Surgery of the Spinal Cord and Column

By M. SCOTT, M.D.

CONGENITAL ABNORMALITIES

GROSS and associates¹⁸ report on 40 infants and children studied in the Childrens Hospital in Boston during a 30 year period ending May 1, 1950 who were operated upon for sacrococcygeal teratomas. They state that these lesions are most frequent in infancy, early childhood and in females and may reach an enormous size compared to the size or weight of the patient. The authors recommend radical removal regardless of size and age or even prematurity of the host. The entire coccyx should always be excised along with the neoplasm because microscopic nests of neoplastic nests are commonly found in or about this bone. There were no operative deaths in their series. Thirty-two of the patients were in the newborn period, 29 of whom were operated upon. Twenty-six of these are alive and apparently cured. Eight were older babies or children and of these three are apparently free of neoplasm. Of the entire group of 40 patients, they report an overall salvage of 29 who are presumably cured. They point out that the outlook is better with these tumors in the newborn group than in the older, and that the majority of these patients can be cured if prompt and adequate surgical removal is done.

The serious prognosis of this tumor in older children is stressed by Ravitch³⁷ and Smith. They report nine cases and of these, three died from metastasis, and in one, there was massive local recurrence. They advocate immediate operation to forestall severe pressure symptoms or metastasis.

Roberts³⁸ reports a case of congenital sacrococcygeal teratoma in a male infant who was operated upon when he was seven hours old. A complete recovery occurred. The author quotes Hundling as stating that these congenital tumors occur in one out of every 34,582 births.

Palumbo³⁴ reports a rare case of a 35-year-old white male who had a huge sacrococcygeal teratoma which contained a glomus. There was complete recovery with no recurrence of the lesion 18 months after the surgery.

According to Slepian and Hamby,⁴¹ hereditary deforming chondrodysplasia is described as a congenital abnormality of osteochondral development, resulting in irregularity and arrest in growth at the metaphyseal

ends of long bones causing deformity and the occurrence of multiple cartilaginous masses which with calcification become osteocartilaginous. Various names have been given to this condition. The most frequently used are hereditary deforming chondrodysplasia, multiple cartilaginous exostosis, dyschondroplasia and diaphysial aclasia. They report that 19 cases of neurologic complications of chondrodysplasia have been found in the literature. Their two cases occurring in brothers make a total of twenty-one. The male sex was involved in 14 of the 15 reported cases in which sex is mentioned. The spinal cord was involved in ten cases, the sciatic nerve in six, the peroneal nerve in two and the brachial plexus and ulnar nerve in one case each.

Teng,⁴⁴ Gross and Newman, report four cases of compression of the spinal cord of unusual etiology. One case was due to Paget's disease of the vertebra. Laminectomy benefited the patient. Two cases of giant cell tumor of the vertebra are reported; one with involvement of the cauda equina, the other with cord compression. Laminectomy resulted in complete recovery of both cases. The fourth case is that of a female age 37 who had polyostotic fibrous dysplasia involving D-7 and D-8 with spinal cord compression. The patient made a complete recovery after laminectomy with recurrence of the paraplegia 15 months later. The authors point out that unlike osteitis deformans, fibrous dysplasia appears to be a congenital disorder of the bone forming mesenchyme. It usually affects children or adolescents and females more than males. It is a rare disease characterized by bone changes, cutaneous pigmentation and sexual precocity and was first described by Albright and his associates. The disease has a tendency to involve bones on one side of the body. When more than one bone is involved it is called polyostotic fibrous dysplasia and, if limited to one bone, monostotic fibrous dysplasia. The authors were unable to find in the literature another case of spinal cord compression due to osteotic fibrous dysplasia.

Extrathecal hemangiolipomas of the spinal canal are rare lesions. Taylor⁴⁵ and his associates report a total of ten cases in the literature including two of their own. Both of their cases occurred in women and a fluctuating course was present in one case in which a period of nine years elapsed from the onset of symptoms; during this time the patient had complete remissions of symptoms on three occasions. At operation the tumor was found to be distinct from the extradural fat and could be easily dissected from the dura. The patients who were paralyzed showed a marked improvement following operation.

Other lesions which may cause intermittent and reversible paraplegia are spinal teratoma. Furtado and Marques¹⁶ report such a tumor in a woman

age 42 years. She had a period of almost complete paraplegia for ten months with spontaneous recovery until she became three months pregnant at which time the weakness recurred. Following the birth of a normal child, she became completely paraplegic. About four months later she regained some of her power and was able to walk about the house with some difficulty. Six months later she became pregnant again and in approximately three months again had an increase in the paraparesis. Following the birth of a second child examination showed spastic paraplegia in the lower extremities with a bilateral Babinski and decrease of sensation below the 4th thoracic dermatome. The posterior columns appeared intact. The blood serology was positive. The spinal fluid protein was elevated and a positive spinal fluid Wassermann and luetic zone colloidal gold curve were present. A myelogram showed a block at D-5 and operation disclosed an ovoid yellowish white tumor which compressed the spinal cord to ribbon size. The tumor was completely adherent to it and an intracapsular removal of caseous material was done. The microscopy showed areas of keratinized epithelial cells and in some sections muscle fibers with few sarcolemma nuclei. In addition, a typical hair as well as a bone fragment in the shape of a terminal phalanx was found. The authors state that a distinction must be made between teratomas and epidermoid tumors. The latter are without neoplastic features while true teratomas almost always contain elements derived from the three germ layers. In adults there is an added cause for an atypical clinical picture, the not infrequent co-existence of teratoma and syringomyelia. (The above cases, and others I have seen, prove that remissions of symptoms can occur in spinal canal tumors as well as in multiple sclerosis and the latter diagnosis should never be made without first ruling out a tumor by contrast media.)

Moore²⁸ and Walker report a case of lumbar intraspinal epidermoid tumor in a male 52 years of age.

TRAUMA TO THE SPINAL COLUMN OR ITS CONTENTS

Schneider³⁹ reports two cases of acute cervical spine injury in which there was immediate complete paralysis with hypesthesia below the level of the lesion and preservation of touch and a part of vibration sense. A ruptured nucleus pulposus was diagnosed in both cases and found at operation. In one case, the ruptured disc was associated with a compression fracture of a cervical vertebra. The author believes that the symptoms in his two cases can be explained on the mechanical stress concept first described by Kahn who emphasized the fixation of the dentate ligament in chronic anterior cord compression. The author lists the indications for early operation of cervical cord injury and, because of his experiences in

these two cases would like to give as another indication for surgery immediate complete paralysis with hypalgesia to the level of the lesion and the preservation of touch throughout the body.

Bors³ studied in detail the phantom sensation of 50 patients with spinal cord injury at various levels, as well as those of seven patients with a combination of damage to the spinal cord and various amputations. The phantom changes in 12 patients following cordotomy were also studied.

The present urologic status of wartime paraplegics is described by Hutch and Bunts.²⁰ Their follow-up covers 170 paraplegic patients with spinal cord injury resulting in neurogenic bladder. An average of four years had elapsed since the injury was sustained. Of the total 170 patients, 142 had a voiding trial and of these, 73 had mild disturbances of bladder function and 69 severe disturbances. The authors believe that the condition of the patients with lower cord lesions was as good as or better than those with higher cord lesions. The 82 patients whose bladders were drained by urethral catheters eventually showed relatively good function in 49 (or 60 per cent) whereas in 51 patients whose bladders were drained by suprapubic catheters only 18 (or 35 per cent) had clinically good function. The commonest causes for failure of the bladder to resume function were peripheral spasms and contracted bladders. The authors also found that functional damage, as judged by excretory urography, was not pronounced during the first three years but then increased rapidly. Such factors as stones and infections were common during the first two years but then became less important.

Pollock³⁵ and his associates have studied spasticity and other reflex activity late after injury to the spinal cord. Their studies center about 300 veterans suffering from injuries to the spinal cord and cauda equina who are in constant residence in the medical wards of the U. S. Veterans Hospital at Hines, Illinois. They found that paraplegic flexion was not related to the severity of the lesion but was related definitely to the level of the lesion and was observed most frequently in injuries of the cervical cord and least in lesions of the lumbar area. As time after injury progressed the posture changed from one in flexion to one in extension.

Down to the level of the 9th thoracic segment, there is no correlation of the level to the presence, increase or absence of the deep reflexes. Below this level the reflexes diminish in number as the level descends. The greater number of segments in the distal end of the injured spinal cord, the greater is the potential total activity. The small number of segments, the fewer are the reflex responses and the more fragmentary are the muscle group contractions.

Long after injury, the reflex activity of the distal segment of a severed or severely injured spinal cord has changed to such a degree that no longer

is it possible by any reflex characteristics to differentiate between complete and incomplete lesions.

Pollock³⁶ and his associates in another article discuss the management of residuals of injury to the spinal cord and cauda equina in the patients mentioned above. They believe that after excluding root pains which occur at the level of the injury, the most common type of pain is a "burning" pain. They believe that they have shown by the use of spinal anesthesia that the site of origin of this burning pain is the distal portion of the proximal segment of the injured spinal cord. They, therefore, feel that posterior root section (rhizotomy), chordotomy and any operation upon the sympathetic nervous system would be futile. They believe that if the patient is given time and surgical procedure withheld that this burning sensation will diminish in severity and recede in consciousness. The authors suggest that severe reflex spasm can be diminished by adequate treatment of bowel and bladder function and by the healing of bed sores. Since anterior rhizotomy results in irreversible loss of power they agree that unless the lesion was proven to be permanently complete that rhizotomy was to be done only on rare occasions when it would be a life saving procedure. The authors discuss in detail the prevention and treatment of decubitus ulcers, bladder dysfunction, bowel control and physical medicine and rehabilitation.

A symposium¹² on the rehabilitation of paraplegics is presented in the May, 1951 issue of the Journal of the American Medical Association. French¹⁵ deals with neurosurgical treatment. In his experience, late laminectomy in patients with traumatic paraplegia has not been encouraging in the return of spinal cord function. He admits that rarely can improvement occur and that the patients accept their condition better after direct verification of the cord injury has been established. They stop hoping for a spontaneous miracle and begin to put more personal effort into the rehabilitation. French favors 5 to 15 cc. of absolute alcohol into the lumbar canal as advocated by Sheldon and Bors in some cases of severe spasms. He is inclined more favorably towards anterior rhizotomy and chordotomy than Pollock and his associates. During the two year period covered by his review, about 500 patients had been studied and treated by the paraplegic service at the Veterans Administration Hospital of Van Nuys. Of these, 77 required neurosurgical operation during convalescence because of a static or regressive rehabilitation status due to various conditions.

The urologic aspects of rehabilitation in spinal cord injuries are discussed by Bors.⁴ The author discusses bladder physiology and routine management of the traumatic cord bladder. He cites the advantages of pudendal nerve operations and transurethral resections in selected cases. The prevention and treatment of complications such as calculosis, epididymitis and urethral pathology are outlined.

Reconstructive surgery in this symposium is described by Comarr,⁷ who states that certain principles govern radical surgery of decubitus ulcers. There must not be excessive spasticity, and the kind of operation is chosen in accordance with the general condition of the patient and the local appearance of clean granulation, rather than by indication of the bacterial count. Penicillin therapy is started 24 hours before intervention. Removal of the entire focus is performed including the bursal fat, diseased osseous tissue and adjoining calcifications. The choice of the skin incision rests with the discretion of the operator. The final article in this symposium on the physical treatment and rehabilitation of the paraplegic patient is given by Dinken.¹⁰

The above group of papers are a challenge to those treating the civilian paraplegic.

HERNIATION OF INTERVERTEBRAL DISCS

Frykholm¹⁷ has published three important articles on the anatomy of the cervical spine and its relation to the cervical disc. The first deals with the lower cervical vertebra and the intervertebral disc. He discusses the pathogenesis of disc protrusion and suggests a new classification for the localized protrusion. The most important are the dorsolateral and the intraforaminal protrusion which both produce radicular compression. In dorsolateral protrusion, the decompression of the nerve roots can be obtained by a simple laminectomy whereas intraforaminal protrusion requires removal of the medial half of the articular facets (hemi-facetectomy). Since hemi-facetectomy restores the horizontal diameter in a constricted foramen, he believes that removal of a hard intraforaminal protrusion is thus not necessary. Although the author believes that roentgenologic narrowing of a disc interspace combined with sclerosis of adjacent vertebral margins is always consistent with a disc protrusion, large protrusions have been observed in interspaces which were roentgenologically normal.

Frykholm's¹⁷ second paper deals with the lower cervical nerve roots, root pouches and root sleeves in detail. The author states that the junction between the dural sac and each radicular nerve is normally formed by a funnel shaped pouch and this prevents the nerve roots from becoming sharply angulated at the point where they abruptly change their course and are, therefore, most susceptible to trauma. A distorted pouch results in sharp angulation of the nerve root. A locus minoris resistentiae is thus established. The roots become subjected to increased strain and traction in the dural lining and this may result in root sleeve fibrosis which may give rise to radicular symptoms. The root sleeve fibrosis may also occur as a result of friction of the nerve with an adjacent pedicle. Frykholm brings out that in a human cervical radicular nerve there is no subarachnoid "cul-

de-sac" as in the lumbosacral nerves. It is, therefore, possible with pantopaque to visualize only the root pouches but not the root sleeve.

In his third article, Frykholm¹⁷ describes the cervical epidural structures, the peri-radicular and epineurial sheaths and their various connections with the spinal column, dural sac, radicular and segmental nerves and plexus trunks. He mentions that the fascia of the posterior longitudinal ligament is continued through the intervertebral foramina and takes part in the formation of the peri-radicular sheath. This helps to counteract outward displacement of the radicular nerve by the fascia. The epineurial sheaths are firmly anchored in the gutters of the transverse processes. The sheaths of the upper plexus trunks are additionally reinforced by ligaments merging from the transverse processes immediately above. When the trunks are subjected to forceful traction the strain falls on these attachments and not on the nerve. If this protecting mechanism fails the strain is transmitted to the peri-radicular sheath with which the epineurial sheaths are continuous. Only if their spinal attachments give away also does the strain fall directly on the nerve. (Frykholm's work is outstanding and is a valuable contribution to those interested in disc anatomy and symptomatology.)

Shenkin and Groff⁴⁰ report a series of cases supporting the concept that pain from a herniated cervical disc may be due, in part, to spasm of the scalenus anticus muscle probably secondary to root irritation. They report four cases relieved by anterior scalenotomy. Only two of the four cases had a myelogram and, in these, a definite defect suggesting disc or exostosis was found.

Mack²⁶ states that electromyographic studies of the sacrospinalis muscle in patients complaining of low back pain following operative removal of a herniated intervertebral disc in the lumbar region have shown evidence of segmental denervation. His report comprises 18 cases including six of severe low back pain associated with sacrospinalis denervation. He attempts to correlate the denervation with the detailed anatomy of the posterior division of the lumbar nerves and to offer a possible explanation of the post-operative back pain on an anatomic basis. In all cases, the improvement or the cessation of pain has paralleled the improvement in the electromyographic recording indicating a return of innervation of the involved muscle segment. The author believes that a stretch injury to the posterior division of the spinal nerve root due to retraction is a cause for this denervation. Mack suggests that this post-operative complication of back pain might be avoided if the operator was careful not to make any unusual traction on the spinal nerve root.

Walker,⁴⁵ Moore and Simpson succinctly discuss the diagnosis and surgical treatment of lesions of the cervical intervertebral discs. Their illustrations graphically bring out the various diagnostic points.

Jefferson²¹ surveys a group of 12 patients who had cervical nerve root disturbances due to ruptured discs. The diagnosis was made on clinical grounds alone in six cases; proven at operation in four; and confirmed myelographically in two others. The average duration of symptoms was eight months and in only one patient was there a history of a definite neck injury. The pain was bilateral in only one case. The total protein was elevated in only two patients and the most frequent sites of the disc lesion were at the C-7 root in seven cases and C-6 root in four cases. Conservative orthopedic measures were recommended in most cases. Four patients had surgical therapy and three of these made excellent recoveries and the fourth had post-operative signs of damage to the spinal cord.

Compression of the spinal cord by protrusion of cervical discs is recorded by Müller³⁰ in 13 patients. Only two patients were aware of any trauma. The clinical picture could be confused with that of tumors and degenerative disease of the spinal cord. Twelve patients were operated upon but the results were not very satisfactory because in a majority of cases irreversible injury of the spinal cord had already occurred.

Strully⁴² and his associates report six cases of compression of the cord due to herniated discs and reveal that previous diagnosis of "degenerative cord disease," "syringomyelia," "multiple sclerosis," amyotrophic lateral sclerosis and combined system disease had discouraged any active therapy. In all the patients the course was progressive and the signs and symptoms could readily be accounted for by lesions below the foramen magnum. Four patients had an elevation of total protein the spinal fluid. In five there was osteoarthritic lipping and a narrow intervertebral space at the level of the lesion. In five, pantopaque myelography of the cervical region revealed a moderate or minimal defect at the level of the lesion. In all six patients the pathologic process was a calcified herniated intervertebral disc associated with osteoarthritic lipping in such fashion as to produce a definite compression and angulation of the cord. Because of the nature of the lesion, surgical intervention was in all but one case limited to freeing cord by cutting the dentate ligament. Although it is too early to record the final results, the authors believe that some improvement has occurred in four patients from three to seven months after operation.

Epstein and Davidoff¹³ state that hypertrophic changes in the cervical vertebra are seen frequently and ordinarily arouse little concern. However, when extensive enough to compress the neural structures a syndrome results which presents many clinical features in common with those of chronic degenerative diseases of the spinal cord such as primary lateral sclerosis, amyotrophic lateral sclerosis and multiple sclerosis. The authors would prefer to call the spine changes hypertrophic spondylitis or more appropriately to indicate the non-inflammatory origin, hypertrophic spon-

dylosis. They describe six cases and emphasize the trauma to the spinal cord produced by the bony hard osteophytes projecting posteriorly into the spinal canal from the vertebral margins in the middle and lower cervical region. In addition, nerve root compression as a result of contraction of the intervertebral foramina produces weakness and atrophy with sensory and reflex disturbances in the upper extremities. The non-inflammatory productive bony changes responsible for the nerve damage and injury are believed to be the result of degeneration of the intervertebral disc. Myelography is mandatory if one is to appreciate the fullest extent of the productive changes characteristic of this disease. The dentate ligament of the cord should be cut to relieve the stress transmitted indirectly to the lateral and posterior column of the cord. They obtained excellent results with this method in two patients.

Kroll and Reiss²³ report 27 cases of prolapse of the thoracic disc. No discs were found in the region of the upper five dorsal vertebra; in eight the affected discs were found protruded between the 11th and 12th vertebrae. Seventeen cases were operated and these comprise 5 per cent of the entire group of 300 disc cases operated on by the authors.

Hirsch¹⁹ has published studies on the mechanism of low back pain. He noted the effect of pressure on discs from fresh autopsy cases. By means of a gear system and measuring device that would record various pressures applied to the disc, he found that when pressure was applied on the vertebra the disc became hard. In the normal group the degree of pressure on the various portions of the disc was identical. However, in those cases with degenerative changes the degree of pressure in different portions of the disc varied greatly. He therefore believes that the cause of rupture in the annulus fibrosis is the decreasing of its resistance to mechanical strain. If the nucleus loses its jelly quality, stresses and strains arise in the surrounding annulus and result in its rupture. Previously he found that if he injected a small amount of saline directly into the disc that the individual would develop back pain which could be prevented by a similar preliminary injection of novocaine. From this he concludes that an increase in the intradisc pressure could cause pressure against the posterior longitudinal ligament, irritate the nerve endings in this ligament and produce the back pain without sciatica.

Charnley⁶ has reported on orthopedic signs in the diagnosis of disc protrusion with special reference to the straight leg raising test. The author believes that the straight leg raising test is more valuable than any other procedure in the diagnosis and prognosis following surgery in patients with herniated discs. He reports 88 patients. Ninety-two per cent of these had a definite limitation of straight leg raising to less than 40 degrees and had a protruded disc, whereas in 25 patients with less limitation on straight

leg raising, only 64 per cent had a protruded disc. A very large percentage of the patients who had excellent results following surgery had a marked limitation of straight leg raising before the operation.

Müller³¹ presents four cases of protrusion of thoracic intervertebral discs. If they occur laterally they may produce radicular pain or be confused with intercostal neuralgia, some type of deep visceral pathology or even angina pectoris. If they protrude in the midline they may produce symptoms of cord compression. In two of his cases, there was calcification in the involved disc and narrowing of the interspace. In the other two there were no significant findings on x-rays. Myelography revealed a complete block in one and a filling defect in three cases. The results following surgery in Müller's group were poor because he attempted to chisel away the hard calcified protrusions which were present in each case. This led to an almost complete paralysis in all his cases which was permanent. Müller no doubt was unaware of the work done in this country on section of the dentate ligament in cases of this type.

Burns⁵ and Young obtained reports from 616 of 832 patients operated upon for protruded lumbar discs between 1940 and 1948. Approximately three fourths of their patients had no pain or disability or only an occasional ache in the back or leg. About 20 per cent had a satisfactory result but still had some pain in the back or leg or both. Ten per cent were not improved. They believe that if the back pain recurs after relief approximately three to four months after the surgery, there has probably been a protrusion of the same disc or another one. Eighteen patients with recurrences came to re-exploration and in every case an additional protrusion was found. A protrusion of another disc was found twice as frequently as a recurrence or an additional protrusion of the previously operated disc. Their results were about half as good in cases without marked protrusion (so-called bulging discs and soft areas).

Kuhlendahl and Hensell²⁴ discuss the results of surgical treatment of prolapsed lumbar intervertebral disc in a group of 210 patients. They believe that decompression of the nerve root is the first and foremost aim of surgical treatment. A follow-up of the 210 cases for a period of more than one to four years revealed complete disappearance of the sciatic and back pain and return to work in 40 per cent of the patients. An additional 25 per cent had good results except for some temporary slight back pain. Thus, 65 per cent of the patients operated upon had satisfactory results. Of the 39 per cent of the patients who were considerably improved, 19 per cent were able to resume their previous work while 11 per cent could only perform light work. Five per cent of their cases were therapeutic failures, mainly because of considerable back pain which prevented return to work and 5 per cent of their patients operated upon had recurrences. They state

that a review of 6,600 patients operated upon and recorded in the world literature showed satisfactory results in some 83 to 95 per cent of the cases.

O'Connell³³ analyzes the results of surgical treatment of 500 cases of proven lumbar intervertebral disc protrusion which he operated between January 1938 and May 1949 at the St. Bartholomew's Hospital. Most neurosurgeons would not agree with O'Connell that it is unnecessary to perform either lumbar puncture or myelography to make a diagnosis. There was a history of definite injury in 59 per cent of the cases and of pregnancy and labor in 5.8 per cent. Although pain was the predominant symptom, 21 of his patients had severe weakness in one or both extremities and five had a clinical picture suggesting marked involvement of the cauda equina. A positive straight leg raising test was present in 99 per cent of the patients. Hemilaminectomy was the surgical procedure and an attempt was made to remove as much as possible of the intervertebral disc.

O'Connell³³ reached the following conclusions: (1) Excision of a lumbar intervertebral disc protrusion is required in only a small proportion of patients with this lesion. (2) A careful clinical and radiologic examination of cases of lumbago and pain in the lower limb provides good evidence not only of the presence of a lumbar intervertebral disc protrusion but also offers anatomic level, size and relationship. (3) In the series, 92 per cent of the patients were either completely free of symptoms or very greatly improved after operation. (4) Persistence of a preoperative neurologic deficit after operation, is however, relatively frequent though seldom disabling. (5) The incidence of postoperative recurrence of symptoms of such severity as to indicate re-operation in the series is two per cent. (This is unusually low. Most authors report about five to eight per cent.)

Barr² summarizes his experiences with low back and sciatic pain covering 18 years and gives the results of treatment. He observes that the size of the myelographic defect, if one is present, has little relationship to the result. (Some neurosurgeons may disagree with this opinion.) He also points out that most observers agree that 30 per cent of patients with disc lesions will recover spontaneously from their first attack. He feels that the greatest single advance in treatment of sciatic pain has been the development of a simple safe operative method of relieving nerve root pressure caused by the protruded disc. He agrees that about 80 per cent of patients are permanently relieved of the acute pain and restored at least partially to satisfactory functional ability. He warns that enthusiasm for the operative procedure must be tempered with good judgment.

Barr² lists the following as the cause of failure after operation: (1) Wrong or incomplete diagnosis. (2) Delay in treatment. (3) Poor selection of cases. (4) Surgical risks and complications. (5) Poorly supervised after-care. He differs with O'Connell concerning myelography and believes that

it is of great value in arriving at an accurate diagnosis and he uses it routinely.

Barr² states that it is not commonly recognized that the removal of an unequivocal disc lesion will fail to relieve the symptoms of a patient who also has a major mental component in the form of fear, anxiety and ill-feeling; however, he believes that the recognition of this factor, frank discussion of the problem and attempted correction of the psychogenic factors when accompanied by properly timed adequate surgery, will yield brilliant results in many otherwise hopeless situations. He lists the operative mortality in most series as being less than one per cent and the postoperative infection as four per cent or less. He points out that if the infection, however, occurs deep in the intervertebral space that this condition is much more serious and difficult to correct. He adds that poor results may occur due to failure to remove completely the displaced disc tissue and also failure to recognize multiple lesions. Another cause for failure is the neglect of proper supervision of the patient after operation particularly for correction of muscle weakness and postural defects. Barr agrees that practically 90 per cent of the patients are usually relieved of sciatica but at least 50 per cent complain of some weakness in their back or some back ache. Barr states: "Thirty to forty per cent of patients at the Massachusetts General Hospital have the combined operation of disc removal followed by fusion. Our staff has been aware of the potential benefit derived from this operation but we have also recognized its technical difficulties."

Barr² previously reported two series of cases from the Massachusetts General Hospital (1941-1947) comparing the results of disc excision and excision-fusion; in both of the series, the combined operation appeared to be *somewhat* better. (See Progress in Neurology & Psychiatry 1948.) In this most recent paper, Barr gives a third series of 495 cases (public and private ones) operated at the Massachusetts General Hospital between January, 1941 and June, 1946. One hundred and sixty-six or 33 per cent had the combined excision and fusion and 329 or 67 per cent had the excision of the disc only. There were three deaths due to operation in the entire series and all of the deaths were in the group which had excision combined with fusion. Thus his mortality rate for the disc excision alone was zero whereas his mortality rate for the combined operation of excision and fusion was 1.8 per cent. The mortality rate for the entire series was 0.6 per cent. The minimum time following operation was five years and the average time following operation eight years. Barr considers this a long time follow-up.

A variety of technics were used for the fusion. It was usually a modification of Hibbs technic and additional bone was removed either from the

iliac area or a tibial graft was used. The "H" or clothes-pin graft (Bosworth) was not used in this series.

The patients who had excision of disc alone averaged 18 days in the hospital after operation whereas the patients who had excision followed by fusion averaged 40 days follow-up in the hospital. There was little difference in complications in both groups. Wound infection or phlebothrombosis occurred in five patients in each series.

In general, patients with fusion were permitted to do heavy work about six months after the operation. In the non-fusion cases whole activity was resumed somewhat earlier either on medical advice or on the patient's own initiative.

Ninety-seven per cent of the patients were relieved of the sciatic pain regardless of whether fusion was done or not. Barr, therefore, believes that this percentage confirms the observation also of others of the efficiency of disc removal alone for the relief of the sciatic pain. However, he states that 80 per cent of the patients with excision and fusion and 64 per cent of the patients with excision alone were essentially free of back symptoms. A total of six patients required re-exploration. Two in the fusion group were recurrent disc and four in the excision group. Although it definitely appears that Barr leans slightly to the combined operation he admits that "indubitable statistical proofs of the superiority of the combined fusion-excision operation is not available. There is additional operative risk in adding fusion to disc excision and it should be omitted in cardiac and other complications. There is obvious need for better techniques in fusion. The incidence of pseudo-arthrosis is much too high."

Armstrong¹ reviews the causes for failure in lumbar intervertebral disc surgery. He states that the poor results reported for 5 to 40 per cent of intervertebral disc operations could frequently be avoided if the hazards were clearly understood. A wrong diagnosis is probably the most frequent cause of unsatisfactory results following operation. He believes that even after earlier unsuccessful operations invalidism can be prevented in some cases by carefully studying the source of difficulty and by further therapy which does not necessarily include spinal fusion. The operation for a definite disc lesion may fail for any one of the following causes: (1) The lesion may not be found. He points out the inadequacy of the interlaminar approach as against the better visualization with hemilaminectomy; even at the proper level the diseased disc may be unrecognized because of inadequate view or bleeding from the extradural veins. (2) Failure to recognize a double lesion. (3) Failure to deal with a bilateral lesion. (4) Subsequent further retropulsion of the nucleus tissue due to incomplete removal at the first operation. (5) Postoperative adherent adhesions causing adherence of the

root to the adjacent tissues. (6) Subsequent prolapse of a previously healthy appearing disc. (7) Permanent changes in the nerve root due to surgery being delayed too long. (8) Damage to the posterior articular facets resulting in an irritable joint which might necessitate arthrodesis. (9) On the other hand, immediate arthrodesis or too early exercise might exaggerate the postoperative pain which always results from uneven pressure from the vertebral body and disorganization of the posterior joint. Armstrong is unequivocal concerning spinal fusion. He feels that it is unnecessary in most cases and may be harmful. The surgical risk is increased and disability greatly prolonged. Re-operation may be much more difficult. He states that if fusion is required that it be done in a second stage. Rehabilitation he believes should never be started before the sixth postoperative week; with adequate rest the symptoms usually subside. (10) Marked adhesions involving the dura and the extradural nerve roots will follow any severe postoperative infection and he suggests that this requires immobilization for several months. (11) Gross injury to the spinal sac, the cauda equina or to the extrathecal roots might result in partial or complete paralysis.

TUMORS OF THE SPINAL CORD

Mosberg²⁹ reports on spinal tumors diagnosed during the first year of life and cites a case of a five month old child who became paraplegic; a laminectomy revealed an extradural thoracolumbar leukemic deposit. (The condition was subsequently diagnosed as lymphatic leukemia.) He quotes 23 previously reported instances in which an intraspinal tumor had been diagnosed during the first year of life. The majority of the tumors were associated with other congenital abnormalities and about 50 per cent were diagnosed by surgery. The pathologic findings were listed as follows: Lipoma—6 cases; dermoid—4; teratoid—4; teratoma—3; sarcoma—3; neurofibroma—1; neuroblastoma—1; and intramedullary glioma—1.

Dodge¹¹ and his associates reveal that low back and sciatic pain even without neurologic manifestations can be due to tumors of the spinal cord. During a two year period, 1,242 patients were operated upon at the Mayo Clinic for herniated lumbar discs. During the same period a diagnosis of suspected protruded disc utilizing the same diagnostic criteria was made in an additional 27 patients who were found actually to have tumors. In the entire group of 27 patients almost 50 per cent or twelve had no sensory, motor, reflex or sphincteric disturbance. Many of the lesions were present at a higher level than suspected and the most common tumors were meningiomas and neurofibromas, although gliomas and ependymomas were also found. They again emphasize the importance of spinal fluid analysis and myelogram so that these tumors might not be missed. A tumor should

always be suspected or considered a possibility as a cause of low back or sciatic pain.

Moersch,²⁷ Craig and Christoferson report on spinal cord tumors with minimal neurologic findings. Out of a group of 150 verified spinal cord tumors, 37 were reported in this study. Of these, 32 exhibited no definite or localizing neurologic signs at the time operation was performed and the remaining five were neurologically negative at the time of their original examination, but developed definite signs while under observation. The only constant symptom in these patients was that of pain which was the primary complaint in all cases. However, the pain was not typical either in character or location and in the vast majority occurred at night, or was increased by lying down and could be induced or intensified by coughing, sneezing or straining. The duration of illness varied from two months to 27 years and the ages of the patients ranged from 11 to 72 years. Roentgenologic examination alone of the spinal column indicated the presence of the tumor in ten of the 37 cases. The spinal fluid protein was elevated in 26 of the 29 instances in which it was studied and myelography was of help in localization of the spinal cord tumor in 90 per cent of the patients.

Thirty myelograms were performed on 28 patients. Air was used as the contrast medial in four myelograms and either iodized oil or pantopaque in the remaining 26 cases. The three unsatisfactory myelograms were all performed with air as the contrast medium and in two cases they were repeated with iodized oil at a later date with satisfactory results. The report of the above authors again emphasizes the importance of spinal fluid analysis and myelography in all patients who have pain of a persistent nature that cannot be explained by any other condition.

Cooper,⁸ Craig and Kernohan present data on 15 extramedullary gliomas along the spinal axis but without any "apparent attachment thereto," and which had not arisen by feeding from a primary intramedullary glial or intracerebral neoplasm. Several of these tumors were believed to be neurofibromas or meningiomas prior to microscopic examination of the neoplastic tissue. The neoplasms were classified as three groups: (1) Intradural, extramedullary gliomas—9 cases; (2) Extraspinal gliomas—4 cases; (3) Intraspinal and extraspinal gliomas—2 cases. The authors point out that five of the intraspinal neoplasms were described as appearing definitely encapsulated and four of these nine tumors were believed by the surgeon to be neurofibromas and one was called a meningioma by the operating surgeon. The authors believe that heterotopic gliomas developed from heterotopic glial tissue and that the tumors reported in this series have originated from subarachnoid and subcutaneous glial heterotopias. Neoplastic changes in this heterotopic "pinched off glial tissue" are believed to result in formation of heterotopic gliomas.

INFECTION OF THE SPINAL CANAL OR ITS CONTENTS

Cope⁹ discusses actinomycosis of bone with special reference to infection of the vertebral column. He reports a total of 66 cases in the literature in the past 70 years including 19 cases of his own. He points out that infection of the spine by this condition is always secondary to an infection of the contiguous tissues. It is distinguished from tuberculosis of the spine by the following: no involvement of the intervertebral disc and involvement of the transverse processes and head of the neighboring ribs; sclerosis is generally mingled with rarefactions. The collapse of a vertebral body and kyphosis as seen in tuberculosis is uncommon. However, large abscesses may be present near the vertebral column. The symptoms depend on what part of the thoracic spine is involved. The treatment is usually the use of penicillin and the sulfonilamides. In some cases, a cure may be effected by giving a million units of penicillin a day for at least several weeks, frequently for several months and in some cases for a year or longer. It may be necessary to use aureomycin, chloromycetin or streptomycin. Roentgenograms may show a lattice pattern of the vertebra. However, if treatment is adequate and effectual the roentgenograms may show dense new bone formed over the affected areas of the spine.

Ley²⁵ et al. report an extensive granuloma of the cervical cord in a child eight years old. The symptoms were those of severe quadriplegia. The child recovered completely following removal of the mass. Study of the tissue revealed the causative organism to be *Torula histolytica*. The authors could find only one case similar to it in the literature.

NEW INSTRUMENTS AND TECHNIQS

Frantz¹⁴ describes an improved spine retractor which is a modification of Jensen's. The turning handle has been replaced by a stainless steel gear at right angles to the turning screw. The curve in the plates is increased to $\frac{3}{8}$ of an inch which fixes the plates more securely under the muscle masses.

Nosik³² reports the closure of a nasal meningocele with tantalum gauze to cover the cranial defect. He suggests its use also in lumbar meningocele where local deficiency does not permit successful repair. The technic is described.

MISCELLANEOUS

Kleinberg²² reports his experiences in scoliosis associated with paraplegia. He has only two cases in his 40 years of orthopedics and cites one in a girl aged 12 who had a paraplegia with moderate deformity at the thoracolumbar junction. A myelogram showed a block and a laminectomy revealed a reduction in the neural canal due to bony deformity. There was marked improvement after surgery. The author gives the following theories

as to the direct and immediate cause of the cord compression: (1) Unequal growth of dura and spinal column. (2) Sudden increase in scoliosis. (3) Anomalous tight dural band (McKenzie and Dewar). (4) Spur of bone in neural canal. (5) Angulation of the cord. (6) Tightness of the nerve roots. (7) Injury.

He states that treatment is either conservative or operative and he quotes McKenzie and Dewar who treated 24 patients conservatively. Of these 11, or about 50 per cent, improved. However, these authors favor laminectomy as soon as possible and this is also Kleinberg's preference.

REFERENCES

- ¹ Armstrong, J. R.: Causes of failure in lumbar disk surgery. *J. Bone & Joint Surg.* 33:31-35, 1951.
- ² Barr, J. S.: Low back and sciatic pain. Results of treatment. *J. Bone & Joint Surg.* 33:663, 1951.
- ³ Bors, E.: Phantom limb of patients with spinal cord injury. *Arch. Neurol. & Psychiat.* 66:610, 1951.
- ⁴ —: Urological aspects of rehabilitation in spinal cord injuries. *J.A.M.A.* 146:225, 1951.
- ⁵ Burns, B. H. and Young, M. D.: Surgery for low back pain. *Lancet.* 260:245-249, 1951.
- ⁶ Charnley, J.: Orthopedic signs in the diagnosis of disc protrusion with special reference to straight leg raising. *Lancet.* 260:186, 1951.
- ⁷ Comarr, A. E.: Reconstructive surgery in spinal cord injuries. *J.A.M.A.* 146: 229, 1951.
- ⁸ Cooper, I. S., Craig, W. McK., and Kernohan, J. E.: Tumors of spinal cord. Primary extramedullary gliomas. *Surg. Gynec., & Obst.* 92:183, 1951.
- ⁹ Cope, U. Z.: Actinomyces of bone with special reference to vertebral column. *J. Bone & Joint Surg.* 33:2-5, 1951.
- ¹⁰ Dinken, H.: Physical treatment and rehabilitation of the paraplegic patient. *J.A.M.A.* 146:232, 1951.
- ¹¹ Dodge, H. W., Svien, H. J., Camp, J. D., and Craig W. McK.: Tumors of the spinal cord without neurologic manifestations producing low back and sciatic pain. *Proc. Staff Meet., Mayo Clin.* 26:88, 1951.
- ¹² Editorial: Surgical treatment of lumbar disk lesions. *J.A.M.A.* 146: 732, 1951.
- ¹³ Epstein, J. A. and Davidoff, L. M.: Chronic hypertrophic spondylosis of the cervical spine with compression of the spinal cord and nerve roots. *Surg., Gynec., & Obst.* 93:27, 1951.
- ¹⁴ Frantz, C. H.: An improved spine retractor. *J. Bone & Joint Surg.* 33:268, 1951.
- ¹⁵ French, J. D.: Neurosurgery in the rehabilitation of paraplegics. *J.A.M.A.* 146:223, 1951.
- ¹⁶ Furtado, D. and Marques, V.: Spinal teratoma. *J. Neuropath. & Exper. Neurol.* 10:384, 1951.
- ¹⁷ Frykholm, Ragnar: Lower Cervical Vertebrae and Intervertebral Discs. *Acta chir. Scandinav* 101: Fasc. 5, 357, 1951 *Ibid* 101: Fasc. 6-, 1951, *Ibid* 102: Fasc. 1, 10, 1951.
- ¹⁸ Gross, R. E., Clatworthy, H. W., Jr., and Meeker, I. A.: Sacro-coccygeal teratomas in infants and children. A report of 40 cases. *Surg., Gynec. and Obst.* 92:341, 1951.
- ¹⁹ Hirsch, C.: Mechanism of low back pain. *Acta Orthop. Scandinav.* 20:261, 1951.

- ²⁰ Hutch, J. A. and Bunts, R. C.: Present urologic status of the wartime paraplegic. *J. Urol.* 66:218, 1951.
- ²¹ Jefferson, M.: Laterally placed cervical discs. Review of 12 cases. *Lancet* 1:129, 1951.
- ²² Kleinberg, S.: Scoliosis with paraplegia. *J. Bone & Joint Surg.* 33:225, 1951.
- ²³ Kroll, F. W. and Reiss, E.: Protrusion of the thoracic disc. *Deutsche med. Wchnschr.* 76:600, 1951.
- ²⁴ Kuhlendahl, H. and Hensell, V.: Indications and results of surgical treatment of protruded lumbar intervertebral discs: Follow-up of 210 cases. *Deutsche med. Wchnschr.* 76:165, 1951.
- ²⁵ Ley, A., Oliveras, C., and Jacs, R.: Torula granuloma of the cervical spinal cord. *J. Neurosurg.* 8:327, 1951.
- ²⁶ Mack, E. W.: Electromyographic observations on the post-operative disc patient. *J. Neurosurg.* 8:469, 1951.
- ²⁷ Moersch, F., Craig, W. Mc., and Christoferson, L. A.: Spinal cord tumors with minimal Neurologic findings. *Neurology.* 1:39, 1951.
- ²⁸ Moore, W. W. and Walker, E.: Intraspinal epidermoid tumor. Case report and discussion. *J. Neurosurg.* 8:343, 1951.
- ²⁹ Mosberg, W. H.: Spinal tumors diagnosed during first year of life with report of a case. *J. Neurosurg.* 8:220, 1951.
- ³⁰ Müller, R.: Protrusion of cervical intervertebral disks with compression of spinal cord. *Acta med. Scandinav.* 139:85, 1951.
- ³¹ —: Protrusion of thoracic intervertebral disks with compression of spinal cord. *Acta med. Scandnav.* 139:99, 1951.
- ³² Nosik, W. A.: The repair of lumbar and cranial meningoceles with tantalum gauze. *J. Neurosurg.* 8:540, 1951.
- ³³ O'Connell, John E.: Protrusion of the lumbar intervertebral discs; A clinical review based on 500 cases treated by excision of the protrusion. *J. Bone & Joint Surg.* 33:8, 1951.
- ³⁴ Palumbo, L. T.: Sacrococcygeal teratoma. Review of literature; Report of a case. *Ann. Surg.* 133:421, 1951.
- ³⁵ Pollock, L. J., Boskis, B., Finkelman, I., Chor. H., and Brown, M.: Spasticity, pseudospontaneous spasms and other reflex activities late after injury to spinal cord. *Arch. Neurol. & Psychiat.* 66:537, 1951.
- ³⁶ Pollock, L. J., Boskis, B., Finkelman, I., Chor. H., Arieff, A., Brown, M., Barber, K. E., Kostrubabla, J. G., Newman, L. B., and Kesert, B. H.: Management of residual of injuries to spinal cord and cauda equina. *J.A.M.A.* 146:1551-1563, 1951.
- ³⁷ Ravitch, M. and Smith, E. I.: Sacro-coccygeal teratoma in infants and children. *Surgery.* 30:733, 1951.
- ³⁸ Roberts, K. D.: Congenital sacro-coccygeal teratoma. Case report. *Brit. J. Surg.* 39:179, 1951.
- ³⁹ Schneider, Richard: Symptoms in acute cervical spinal injuries for which early operation is indicated. *J. Neurosurg.* 8:360, 1951.
- ⁴⁰ Shenkin, H. A. and Groff, R. A.: Herniations of cervical intervertebral disc and scalenotomy. *Surgery.* 29:540, 1951.
- ⁴¹ Slepian, A. and Hamby, W. B.: Neurologic complications associated with hereditary deforming chondrodysplasia. Review of the literature and a report on two cases in same family. *J. Neurosurg.* 8:529, 1951.
- ⁴² Strully, K. J., Gross, S. W., Schwartzman, J., and Von Storch, T. J. C.: Progressive

spinal cord disease. Syndromes associated with herniation of cervical intervertebral Disks. *J.A.M.A.* 146:10, 1951.

- ⁴³ Taylor, J., Harries, B. J., and Schurr, P. H.: Extrathecal haemangiolipomas of the spinal canal. *Brit. J. Surg.* 39:1, 1951.
- ⁴⁴ Teng, P., Gross, S. W., and Newman, Chas.: Compression of spinal cord by osteitis deformans (Pagets disease), giant-cell tumor and polyostotic fibrous dysplasia (Albright's syndrome) of the vertebrae. A report of 4 cases. *J. Neurosurg.* 8:482, 1951.
- ⁴⁵ Walker, E., Moore, W. W., and Simpson, J.: The diagnosis and surgical treatment of cervical lesions of the intervertebral disc. *J. Internat. Coll. Surgeons.* 15:411, 1951.

Cerebral Trauma and Traumatic Infection of the Central Nervous System

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PENETRATING CRANIOCEREBRAL WOUNDS

AT A neurosurgical center in Saigon, Arnaud¹ made a follow-up study of 97 cases of penetrating craniocerebral wounds. The statistics were presented 18 to 36 months after operation. Chronic suppuration occurred in 44 per cent of the cases in Indo-Chinese and 22 per cent in Europeans and was usually due to osteomyelitis. Immediate operative treatment of penetrating craniocerebral wounds was not advised, it being considered better judgment to delay operation four to five days or longer. In the first 51 cases who were immediately operated upon, the mortality was 23½ per cent, while in the remaining 46 cases in whom operation was delayed, the mortality was reduced to 11 per cent.

Ritchie Russel² reviewed 1,166 cases of craniocerebral traumas particularly with reference to disability after a five-year follow-up period. Of these, 820 cases penetrated the brain and dura. There were a total of 71 (6 per cent) deaths and an amazingly low incidence of delayed deaths which was attributed to good neurosurgery and antibiotics. There was a high incidence of focal signs immediately after injury in both penetrating and non-penetrating groups. Amnesia was absent in many cases. The very high incidence of early focal signs was believed to be due to spread of a shock-like effect from the site of wounding. Svien³ gives a practical resumé of the management of acute injuries of the brain. The importance of a free airway, oxygen therapy and good nursing care is stressed.

Barré et al.⁴ describe an interesting case in whom the medial angle of the orbit was penetrated by a foil. Four days after injury, the patient (male aged 25) showed pronounced cerebellar, sensory and vestibular disturbances. The cerebrospinal fluid was bloody. Two years after injury, the neurologic picture was unchanged. Hooper⁵ has written an excellent paper on the orbital complications of penetrating cerebral injuries. Fifty-eight cases were studied; 33 (57 per cent) showing deterioration of vision; 19 (33 per cent) double vision; and 19 (33 per cent) displacement of the globe. Deterioration of vision was attributed to neuromuscular paralysis with

loss of accommodation, intra-ocular hemorrhage, or injury to the optic nerve or chiasm. The visual disturbance varied from blurring to complete loss. The mode of onset was usually instantaneous. The author stressed early and repeated examinations since venous distention and blurring of disc margins appeared early and lasted but three to seven days following which these changes receded and were replaced by a typical optic atrophy over a period of three to five weeks. Visual derangements were due to laceration of the intra-orbital section of the nerve by fragments of the orbital roof, fracture of the optic canal or anterior clinoid process, torsion or traction of the optic nerve by displacement of the cerebrum within the skull. Operation was advocated in all cases showing a progressive deterioration of vision. Diplopia was due to paresis of the extrinsic ocular muscles in 75 per cent of the cases and to displacement of the globe in 25 per cent. Many of the cases with initial diplopia following injury fuse images so that few have permanent disability. However, where diplopia was due to deformity of the orbit with globe displacement, operative intervention was required (elevation of the zygomatic bone; lateral orbital exposure; transfrontal craniotomy).

COMPLICATIONS OF CEREBRAL WOUNDS

Post-Traumatic Epilepsy

The paper by Ritchie Russell² indicates the incidence of seizures in 820 cases of penetrating wounds. 356 cases (43 per cent) had one or more seizures within the first five years of wounding while 403 cases did not have seizures over a period of five years. The remaining cases (61) which were followed for a five-year period likewise had no seizures. The site of wounding was charted on a skull map, it being shown that all parts of the cerebrum were implicated. However, the greatest incidence was found to be over the parietal region. In 252 cases out of 358, convulsive seizures made their appearance before a two-year period after wounding.

Dany and Singer⁶ report six cases of post-traumatic epilepsy with acute deliriant psychopathy. A cure was effected by surgical excision of the epileptogenous zone.

Extradural Hemorrhage

Guillaume and Pecker⁷ indicated the clinical symptomatology in a group of cases which they designated as basilar hematoma. In five such cases, oculomotor nerve paralysis was associated with psychic disturbances characterized by confusion, coma, and psychomotor agitation. Ventriculography suggested a tumor of the temporal pole with displacement of the third ventricle. Obliteration or elevation of the temporal horn was also demonstrated. Surgical exploration of the temporal fossa disclosed an extradural

hemorrhage in four of the five cases. In the remaining case the hemorrhage was subdural. It was stated that all recovered from the third nerve paralysis as well as the psychiatric symptoms.

Klingensmith and Voris⁸ reviewed their operative experiences in the treatment of extracerebral hematomas. Fifty-six cases were studied over a 15 month period (1948-1949). The mortality rate was as follows:

31 cases operated first three days after injury—74 per cent

8 cases operated three to seven days after injury—75 per cent

17 cases operated one week after injury—35 per cent

The authors believed that these cases were not always suitable for surgery. Almost invariably, there was associated an extensive laceration of the brain.

Subdural Hemorrhage

The problem of the surgical treatment of acute subdural hemorrhage has again been raised by Chambers.⁹ The author points out the not infrequent occurrence of massive bleeding from the inferior cerebral veins and dural sinuses and is firm in his belief that all these cases should be explored in an attempt to arrest the source of bleeding. A surgical approach is described which permits one to adequately expose the origin of the torn vessel. Two illustrative cases are described. Meredith¹⁰ reports two very unusual cases of subdural hemorrhage occurring after an indirect cranial trauma. Both occurred after a fall on the gluteal region and both recovered following evacuation of a left sided chronic subdural hematoma.

New light has been cast upon the EEG diagnosis of subdural hematomata by Sullivan et al.¹² and Friendlander.¹¹ Friendlander reports on the EEG findings in 39 surgically proven subdural hematomata which included 17 personally observed cases. The cases were classified into 6 groups; (1) normal, (2) diffuse, non-focal slow, (3) focal, low voltage without an abnormal amount of slow, (4) focal, abnormal, low voltage slow, (5) focal, abnormal, slow which amplitude is equal to or greater than the base line voltage on the opposite side and (6) focal, low voltage without an abnormal amount of slow but with high voltage surrounding it. It was interesting to note that six cases with a predominantly unilateral hematomata showed abnormal EEG's with the abnormality on the side opposite the lesions. Twenty patients showed slow activity whose amplitude was equal to or greater than the voltage elsewhere. These specific findings were present in 56 per cent of the cases while some type of focal abnormality which helped in localization of the lesion was found in 67 per cent. Some form of abnormality was found in 92 per cent. Only three patients showed depressed voltage over the site of the hematoma. Sullivan et al.¹² studied 32 cases of surgically

verified subdural hematomata, the majority of the cases being chronic. It was not thought advisable to classify these cases into more than two groups, namely: (1) suppression of alpha activity on the side of the lesion (15 out of 26 unilateral hematomata and hygromata), and (2) slow wave activity of either low or increased voltage (11 unilateral and 2 bilateral hematomata). They were of the opinion that suppression of alpha activity was a specific effect so that correct localization was possible in 47 per cent of the cases and correct lateralization in 75 per cent. As in the cases studied by Friendlander,¹¹ there was a high incidence of abnormality (90 per cent). However, Friendlander makes no reference in his cases to a suppression of alpha activity. Sullivan and his co-workers attribute the suppression of alpha activity to impairment of the cortical blood supply. Perhaps the paper by Browder and Rabiner¹³ may be of some interest in connection with the EEG interpretation in subdural hemorrhage. In subdural hemorrhage, the authors describe a subcortical swelling which they believe to be the dominant factor in the production of the clinical picture. Frequently the brain under the collection was depressed but normal to gross appearances while the surrounding convolutions and sulci were flattened. The finding of slow activity over the site of a subdural hematoma may possibly be explained on the basis of an underlying cerebral edema. Dawson et al.¹⁴ stressed the importance of serial EEG's in 45 cases of cerebral trauma. A lag was frequently found in the appearance of abnormality as long as 48 hours after injury. It was shown that a lethal trauma may have a normal record except for focal changes for several hours. Focal suppression was found to be quite common and was found to correspond to the area of greatest injury. A generalized suppression appearing within 30 hours of the trauma was found to be uniformly fatal.

Other Complications

Yuhl et al.¹⁵ report a patient who had recurrent cerebrospinal rhinorrhea for a period of four years following a penetrating wound of the frontal bone with extension into the orbit. Ten days following a second trauma, a roentgenogram of the skull revealed air in the cerebral ventricles. The patient recovered following operation. Gros and Cazaban^{15a} report a case with a basilar fracture of the frontal bone resulting in cerebrospinal fluid rhinorrhea, bitemporal hemianopsia, complete anosmia, diabetes insipidus (3000 cc. urine passed daily). Roentgenograms disclosed a large pneumatocele just above the floor of the frontal fossa. The opening in the dura was closed and 12 days after operation, the air had disappeared as disclosed by x-ray.

CRANIOPLASTY

Enria and Ferrero¹⁶ have introduced the possible use of bone paste in the repair of cranial defects. Four groups of dogs were studied:

Group I—Cranial defect filled with powdered bone plus blood.

Group II—Cranial defect filled with powdered bone plus blood plus 300,000 units of vitamin D.

Group III—Cranial defect filled with powdered bone plus 300,000 units of vitamin D.

Group IV—No paste used.

The animals were sacrificed at 20, 40, and 60 day intervals following cranioplasty. The best results were obtained in Group I. The bony edges appeared irregular, indistinct and were fused with newly formed bone of the paste inlay. In one animal, the bony defect was totally occupied by a bony opacity. Roentgenograms after 40 and 60 days revealed the cranial defect to be filled with a homogeneous bony matrix. Twenty days after cranioplasty the bone surrounding the defect showed the presence of newly formed bone. The paste inlay was said to have shown active regeneration of bone with centers of ossification in various stages of development. From the practical standpoint it is difficult to see how the normal contour of the skull could be re-established with such a pasty material. Certainly it would be difficult to reform an orbital ridge with this material. Perhaps it may be of value in repair of small defects. The reviewer has used this method with moderate success in the filling of the anterior burr opening in trans-frontal craniotomies.

McClintock and Dingman¹² have again raised the question of repair of cranial defects using autogenous bone (iliac crest). The writers claim that the iliac transplant is much easier to fashion than plates particularly in the repair of orbital ridge defects. They state that plates spring or slip which is not the case with autogenous bone transplants. Air and angiographic studies are also possible whereas metallic plates cast interfering shadows. Metallic plates cause discomfort in extreme degrees of temperature but this does not occur with bone repairs. One of the major objections, of course, is the fact that two major operative procedures are required. The reviewer has found stainless steel (.015 thickness) to be quite easily fashioned at the operating table and quite satisfactory in the repair of cranial defects (see PROGRESS 1951, page 309). This opinion is likewise expressed by Adelstein¹⁸ who has reported the use of stainless steel in the repair of cranial defects in 13 cases. The author has not found it necessary to remove a plate in any of his cases.

CONTUSION

Courville²⁰ has brought forth new light concerning the mechanism of contrecoup injuries of the brain. He argues that subfrontal and temporal contusions are due not to movement of these structures but rather to their failure to move over the interior of the skull and, therefore, dissipate the effects of the blow.

A very important group of cerebral lesions due to blunt trauma studied by autopsy has been reported by Krauland.²¹ Seventeen cases of 124 autopsies were carefully studied microscopically and macroscopically. Petechial hemorrhages were usually caused by rupture of small arteries or veins. Contrecoup lesions were prevalent in the region of the temporal and frontal poles and in the gyrus hippocampi (herniation through the incisura tentorii). Pressure against the falx is responsible for petechial hemorrhages of the gyrus cinguli. Severe lateral blows to the skull may cause tearing of the corpus callosum because the falx cerebri fixes the cerebral cortex while the deeper parts shift to the other side.

POST-CONCUSSION SYNDROME

Kamman²² has stressed the importance of a third post-traumatic concussion entity as contrasted to post-traumatic neurosis and compensation neurosis. This condition is labeled as attitudinal pathosis. In these cases the patients do not have the reactions of a true neurosis and the question of compensation is not a factor. Attitudinal pathosis is a form of personality disorder in which the patient consciously behaves in a certain way because he believes he is right. His emotions are disturbed secondarily by a feeling of resentment which is the principle reaction. Kamman²² recommends a careful study of the post-traumatic personality so that it may be separated from the cerebral traumatic symptomatology. Symptomatology occurs in a pure form only in those cases in which the brain and the entire bodily and mental structure is completely normal before trauma.

TRAUMATIC INFECTION OF THE CENTRAL NERVOUS SYSTEM

Neill and Segerberg²³ studied the bacteriologic flora of penetrating cerebral wounds. Infection with gram negative bacillus, especially the *Klebsiella* group, proves to be the most fatal. Aureomycin and streptomycin were considered the antibiotics of choice. It was routine practice to excise the abscess and close without drainage. Munro,²⁴ reviewing the progress of neurosurgery from 1941 to 1950, remarked that the mortality of brain abscesses has fallen from 53 per cent (1926 to 1940) to 15 per cent in recent years. The use of thorotrast to localize the encapsulated abscess is highly recommended. Huber²⁵ described ten cases of post-traumatic brain ab-

scesses with few or no symptoms until some time had elapsed (two months to one year). In all ten cases the usual diagnostic methods had failed (no mention is made of EEG) and close clinical observation was the deciding factor in diagnosis. The lack of symptomatology was explained by the fact that a penetrating cerebral wound renders the cranium no longer a closed space so that increased intracranial pressure does not develop. None of the ten cases showed papilledema.

A very unusual case of blast injury was reported by Fontan and Marchand.¹⁹ The patient was semi-comatose for three weeks and showed no evidence of a penetrating injury. There was a hemiplegia and a hemianopsia. An exploratory operation revealed an occipital lobe abscess. An explanation for this operative finding could not be found.

Two brain abscesses due to unusual infections were reported by Pilcher²⁶ and by Steen and Thjotta.²⁷ Pilcher's case was a brain abscess due to *nocardia asteroides* while the latter authors reported a case of cerebral abscess due to *bacteriodes serpens*. A cerebral abscess associated with thrombophlebitis of the sinuses was described by Laurence.²⁸

By far the best report on cerebral abscesses was that written by Cuneo.²⁹ The author reviewed 100 consecutive cases paying particular attention to the essential pathology and the causes of mortality.

REFERENCES

- ¹ Arnaud, M.: Long term results of treatment of cerebral wounds in the neurosurgical center in Saigon. *Marseille Chir.* 23:438-447, 1950.
- ² Russel, R. W.: Disability caused by brain wounds. *J. Neurol., Neurosurg. & Psychiat.* 14:35-40, 1951.
- ³ Svien, H. J.: Management of acute injuries of the head. *Wisconsin M. J.* 49:135-138, 1950.
- ⁴ Barré, J. A., Girier, and Hein: Neurological sequelae of an injury at the median angle of the orbit caused by a foil. *Rev. neurol.* 83:298-300, 1950.
- ⁵ Hooper, R. S.: Orbital complications of head injury. *Brit. J. Surg.* 39:126-138, 1951.
- ⁶ Dany, A. and Singer, L.: Post-traumatic epilepsy with acute recurring deliriant psychopathy, hallucinations and attempted suicide cured by excision of the damaged zone. *Strasbourg Méd.* 1:16-20, 1950.
- ⁷ Guillaume, J. and Pecker, J.: The basilar hematoma. A special form of intracranial post-traumatic hematoma. *Presse méd.* 59:345, 1951.
- ⁸ Klingensmith, W. and Voris, H. C.: Surgical treatment of extracerebral hematoma in acute craniocerebral injury. *Am. J. Surg.* 81:533, 1951.
- ⁹ Chambers, J. W.: Acute subdural haematomata. *J. Neurosurg.* 8:263-268, 1951.
- ¹⁰ Meredith, J. M.: Chronic or subacute subdural hematoma due to indirect head trauma. Report of two cases. *J. Neurosurg.* 8:444-446, 1951.
- ¹¹ Friendlander, W. J.: The electroencephalographic findings in 39 surgically proven subdural hematoma. *EEG. & Clin. Neurophysiol.* 3:59-62, 1951.
- ¹² Sullivan, J. F., Abbott, J. A., and Schwab, R. S.: The electroencephalogram in

- cases of subdural hematoma and hydroma. EEG. & Clin. Neurophysiol. 3:131-140, 1951.
- ¹³ Browder, J. and Rabiner, A. M.: Regional swelling of the brain in subdural hematoma. *Ann. Surg.* 134:369-375, 1950.
- ¹⁴ Dawson, R. E., Webster, J. E. and Gurdjian, E. S.: Serial electroencephalography in acute head injuries. *J. Neurosurg.* 8:613-630, 1951.
- ¹⁵ Yuhl, E. T. and Estridge, M. N.: Traumatic pneumocephalus. A brief review with report of case. *Bull. Los Angeles Neurol. Soc.* 15:93-97, 1950.
- ^{15a} Gros, C. and Cazaban, R.: Post-traumatic chiasma syndrome with intracranial pneumatocele. *Presse méd.* 51:398, 1950.
- ¹⁶ Enria, G. and Ferrero, R.: The possibility of the use of bone paste in plastic repair of cranial defects. *Chir. d. org. de mouvements.* 34:459, 1950.
- ¹⁷ McClintock, H. G. and Dingman, R. O.: Repair of cranial defects with iliac bone. *Surgery.* 30:955-963, 1951.
- ¹⁸ Adelstein, T. J.: Stainless steel cranioplasty. *Bull. Los Angeles Neurol. Soc.* 16:185-193, 1951.
- ¹⁹ Fontan, M. and Marchand, M.: Role of blast injury in an accident while clearing a minefield. *Ann. méd.* 30:92-94, 1950.
- ²⁰ Courville, C. B.: The mechanism of coup-contrecoup injuries of the brain. A critical review of recent experimental studies in the light of clinical observations. *Bull. Los Angeles Neurol. Soc.* 15:72-86, 1950.
- ²¹ Krauland, W.: Brain lesions due to blunt trauma. *Deutsche Ztschr. f. Nervenhe.* 163:265-328, 1950.
- ²² Kamman, G. R.: Traumatic neurosis, compensation neurosis or attitudinal pathosis? *Arch. Neurol. & Psychiat.* 65:593-603, 1951.
- ²³ Neil, C. L. and Segerberg, L. H.: Infections of the brain following penetrating wounds. *South Med. & Surg.* 16:341-367, 1950.
- ²⁴ Munro, D.: Medical progress. Neurosurgery. *New England J. Med.* 242:702-715, 1950.
- ²⁵ Huber, K.: Post-traumatic brain abscess without symptoms. *Wien med. Wchnschr.* 101:126, 1951.
- ²⁶ Pilcher, E. K.: Brain abscess due to nocardia asteroides. *Texas State J. Med.* 46:915-919, 1950.
- ²⁷ Steen, E. and Thjotta, T.: Studies on bacterioides V. Cerebral abscess caused by bacterioides serpens. *Acta path. et microbiol. Scandinav.* 27:851-864, 1950.
- ²⁸ Laurence, G.: Abscess of the brain and thrombo-phlebitis of the sinuses. *J. Prat. Par.* 65:161-164, 1951.
- ²⁹ Cuneo, H. M.: Abscess of the brain: a review of the essential pathology in 100 consecutive cases; with some remarks on causes of mortality. *Bull. Los Angeles Neurol. Soc.* 16:162-173, 1951.

Brain Tumors

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IN THE field of brain tumors, the most significant contributions during the past year were those dealing with the use of radioactive substances, primarily for localizing purposes. While it would undoubtedly be premature at this time to attempt a critical evaluation of the usefulness of the radioactive technic the evidence thus far leads to the impression that it holds considerable promise as a diagnostic adjunct. Whether further technical improvements will enhance its value, relative to pneumoencephalography, electroencephalography and angiography, remains to be seen. Probably it will supplement rather than replace any of these established diagnostic methods. The therapeutic potentialities of radioactive substances are also being explored. The results of such studies are awaited.

GENERAL DATA

The tendency of many types of brain tumors to select preferential sites of growth, to affect particular age groups and often to show a relative sex preponderance was again emphasized by Zülch¹⁰² who applied the term "pathocllisis" to these phenomena.

An account of the end results of 802 cases operated upon between 1931 and 1941 at the University of Pennsylvania was described by Grant and Sayers.⁴³ Twenty per cent of all patients were alive in 1950 and 24 per cent had survived 10 or more years following operation. Of 143 cases of cerebral astrocytoma, there were 15 survivors in 1950 and in the group of 84 cerebellar astrocytomas, 18 remained alive. The figures for the other types of tumor were as follows: 142 meningiomas, 47 alive in 1950; 80 pituitary adenomas (55 chromophobe, 17 eosinophile, 8 mixed), 33 alive; 50 medulloblastomas, one alive; 38 acoustic neurinomas, 7 alive; 33 craniopharyngiomas, 8 alive; 19 subtentorial hemangiomas, 11 alive; 18 ependymomas, 4 surviving. None of the 14 patients with an oligodendroglioma were alive after this time had elapsed. Of the 142 cases of glioblastoma and 42 of metastatic carcinoma, there were no five year survivals.

Horrax and Wu⁶⁰ analyzed a series of 26 cases of oligodendroglioma, representing 3.8 per cent of all gliomas observed at the Lahey Clinic. There

were 17 males and 9 females. The average age was 39 years and the average preoperative duration of symptoms 29 months. Calcification was visible in the roentgenograms of nine patients. Twenty tumors were situated in the hemispheres, seven being frontal and five frontotemporal in location. In two cases the lesion was intraventricular and in four the cerebellum was involved. There were four deaths following operation. The average post-operative survival was over seven years; seven patients lived five to ten years, two lived 18 years and one 33 years; six were still alive 19 to 216 months after operation. The authors are of the opinion that the most satisfactory results follow radical tumor surgery.

A detailed analysis of 140 cases of cerebellar astrocytoma treated in Olivecrona's clinic was undertaken by Ringertz and Nordenstam.⁸³ A predominance of polar spongioblasts rather than astrocytes characterized the vast majority of these cases. This finding corresponds to the description of these tumors by Bergstrand and by Zülch. In only six cases was there an abundance of astrocytes leading the authors to conclude that only a minority of benign cerebellar gliomas exhibit the same histologic structure as the hemispheric cerebral astrocytomas. The implication of this finding as regards biologic behavior is further indicated by the authors' observations that the survival of patients with cystic polar spongioblastomas of the cerebrum, similar in structure histologically to that of the cerebellar tumors, was considerably greater than that of patients with the ordinary hemispheric astrocytomas. The 140 cerebellar tumors represented 8.1 per cent of all intracranial gliomas and about half of the gliomas encountered in the posterior fossa. As regards location, 71 were in the midline, 24 were laterally placed and 45 involved both sites. Cysts were present in 110 cases. The mean age was 14.8 years; 71 per cent of patients were 20 years of age or younger. The mean preoperative duration of symptoms was 18.4 months. There was only one recurrence in the group in whom a total removal was believed to have been accomplished. Of 18 patients in whom only a partial removal was performed, ten were well 3 to 16 years after operation. The case mortality was 28.8 per cent.

Two series of colloid cysts of the third ventricle were reviewed. According to Kelly,⁵⁴ who analyzed 29 cases, this type of lesion may manifest itself clinically in one of three ways: (1) as a problem in localization in a patient complaining simply of headache and disclosing on examination primarily papilledema, and possibly false localizing findings as ataxia, and pyramidal and extra-pyramidal signs; (2) as a progressive or fluctuating dementia with or without headache, and with or without evidence of increased intracranial pressure; and (3) in the form of paroxysmal attacks of intense headache relieved or aggravated by postural change, and accompanied by nausea and vomiting, vertigo, transient pareses of the limbs, alteration in con-

sciousness or marked mental changes, the patient being completely devoid of symptoms between episodes. Apart from headache, the most frequently repeated symptom was sudden weakness of the lower extremities resulting in falling without loss of consciousness. Kelly further stated that fits were a rare phenomenon and that in about a third of the cases, there occurred attacks of unconsciousness. In only 8 of the 29 cases were the fundi normal. The patients ranged in age from $21\frac{1}{2}$ to 52 years and most had had symptoms for six months or less at the time of hospitalization. There were 18 males and 11 females. Nine patients died, five following operation and four after ventriculography or ventricular drainage. While it is impossible to establish the diagnosis of a colloid cyst of the third ventricle without resorting to ventriculography, Kelly believes that its presence may be suspected on clinical grounds. A paper by Cairns and Mosberg¹⁸ on the same subject is based on a study of 19 patients. The symptomatology in these cases was due mostly to hydrocephalus, the variation in the clinical picture being attributed to the acuteness of obstruction of the foramen of Monro. Intermittent symptoms occurred in about half of the cases. Hypersomnia was noted in some patients and occasionally glycosuria during an acute hydrocephalic attack. The tumor was removed from 11 patients, nine of whom survived. Eight of the latter were relieved of all symptoms. A transcortical approach is recommended. In cases in which the ventricles are relatively small, a two-stage operation is advised, the frontal dura being opened at the initial procedure to allow the anterior horn to dilate, thereby facilitating entrance into the ventricle at a subsequent session.

Details of a symposium⁹⁷ on the results of treatment of acoustic nerve tumors held at a meeting of the Society of British Neurological Surgeons in 1948 were published. Accounts of the experiences of Horrax and of Olivecrona, both of whom favor radical excision whenever feasible, have already been described in previous reviews. Horrax⁹⁷ reported an operative mortality of 10.9 per cent in 73 cases, in which the tumor was totally removed. The mortality of patients in whom a radical removal was accomplished was 14 per cent after five years, whereas in the group in which an intracapsular excision was performed, this figure was 56 per cent. There were nine postoperative deaths in a series of 85 cases of intracapsular removal reported by Pennybacker and Cairns;⁹⁷ 14 required further operation within four years and of these, half died postoperatively; 40 patients were at work after periods varying from less than two years to ten years after operation. Of the 25 cases in which the tumor was completely removed, four died postoperatively. Twelve of the 17 patients in whom a follow-up was available had resumed normal life for periods ranging from one to 15 years. While favoring the radical operation, especially in younger patients, Pennybacker and Cairns were of the opinion that in older people, a subtotal

removal might often be preferable. In Northfield's⁹⁷ series of 47 patients on whom 57 operations were performed, the case mortality was 38 per cent and the operative mortality 32 per cent. A partial removal was accomplished in 14 cases, 11 of which survived. Of these, five required further operation within four years. Of the 25 patients in whom the tumor was completely removed, 19 survived and of these 11 are gainfully employed; seven made good recoveries and only one remains disabled. The overall mortality in Jefferson's⁹⁷ series of 142 cases was 26 per cent; the tumor was totally extirpated in 34 patients and in this group, the mortality was 8.8 per cent.

Petit-Dutaillis and Daum⁷⁷ described their experience with meningiomas of the posterior fossa. The outlook in cases of convexity meningiomas arising for the most part from the inferior surface of the tentorium and adjacent sinuses was considerably better than that of cases in which the tumor took origin from the base.

The enchondromas of the base of the skull were reviewed by Klinger⁵⁸ who gathered 26 cases from the literature and added five that had been observed in Kraysenbühl's clinic. Of the latter, one involved the clivus, another the petrous apex and cerebellopontine angle and a third was parasellar; in the fourth case the sella was destroyed and the optic chiasm compressed by the tumor which originated in the ethmoid; in the remaining case, the lesion, presumably of ethmoid origin, invaded the orbits and anterior cranial fossa. Multiple cranial nerve involvement, especially trigeminal and abducens paralysis, were the outstanding clinical features. Roentgenograms disclosed destruction of bone and calcification within the tumor. The outlook in this type of tumor is generally unfavorably, surgical treatment being possible only in selected cases.

Störtebecker⁹⁸ presented a study of 19 metastatic cerebral hypernephromas, most of which apparently were solitary lesions. The operative mortality in 17 cases was 30 per cent, and the postoperative period of survival varied from two and a half months to 14 years. In view of the relatively favorable prognosis, active neurosurgical intervention is recommended.

Ten histologically verified cases of cerebral cysticercosis were reported by Obrador and Ley.⁷³ There was evidence of increased intracranial pressure in nine; focal signs were lacking in seven. The ultimate results were poor owing to the multiplicity of lesions.

The 159 cases of tuberculoma of the brain observed at the Neurosurgical Institute in Santiago, Chile over a period of about ten years constituted the subject matter of a paper by Asenjo, Valladares and Fierro.⁶ Histologic verification of the lesion was obtained in 97. The ages of the patients varied from 19 months to 70 years. Extranural tuberculosis was present in 86

cases. Increased intracranial pressure, the most important factor as regards symptomatology, was greatest in patients with tuberculoma of the posterior fossa or with multiple lesions. Surgical treatment combined with the use of streptomycin, paraaminosalicylic acid and promin is advised. Whenever possible the lesion should be removed; otherwise an attempt should be made to relieve the hydrocephalus. Of ten patients treated surgically and to whom streptomycin was administered, only two died.

Pituitary function was studied in 14 patients with chromophobe adenomas and craniopharyngiomas by Paschkis and Cantarow.⁷⁴ The degree of hypopituitarism varied from one extreme to the other and was unrelated to the extent of mechanical neurologic damage produced by the tumor. The secretion of the various pituitary hormones was not impaired to the same degree, leading to various combinations of hypothyroid, hypoadrenocortical and hypogonadal manifestations. Individual adrenal cortical functions were not always all affected, nor to the same extent. The frequency of occurrence of subclinical deficiencies, especially of the adrenal cortex in cases of pituitary tumor, led to the suggestion that appropriate studies be instituted and that adrenocortical hormone be administered where indicated.

The cardiovascular status of 21 acromegalics was investigated by Hejtmancik, Bradfield and Herrmann.⁴⁸ Thirteen had evident heart disease; five were in cardiac failure; two had transient episodes of left ventricular failure; six were hypertensive; the basal metabolic rate was elevated in four; five were diabetic, and nine of 15 examined electrocardiographically had abnormal tracings. Pathologic study of four patients revealed myocardial hypertrophy with conspicuous diffuse fibrous tissue proliferation in two. The secretion of the anterior pituitary would appear to be directly responsible for the cardiac hypertrophy and interstitial fibrosis, other factors such as the increased work demand of the enlarged tissues being contributory.

The finding of a cavernous angioma of the choroid plexus of the lateral ventricle in a three-day old infant led Arnstein, Boldrey and Naffziger⁵ to survey the literature on brain tumors occurring during the neonatal period. Thirteen such cases were found, in none of which was the diagnosis definitely established during life. The tumors were more frequently supratentorial and about half presumably were gliomas; five belonged to the dermoid or teratoid group. The existence of these lesions during this early period of life lends support to the "embryonal rest" theory of their etiology.

An increased urinary excretion of nitrogen and a negative nitrogen balance were reported by Cooper, Ryneerson, MacCarty and Power²³ during the first five postoperative days in patients undergoing craniotomy

for brain tumor. This was less marked in patients to whom testosterone was administered.

PATHOLOGY

According to Cooper and Kernohan²² heterotopic glial nests in the sub-arachnoid space result from the protrusion and pinching off of mature glia from the neuraxis. Most frequently this occurs at the level of the medulla; the second most common site is the lumbosacral region. Rarely these cells come to lie extraspinally. It is likely that primary extramedullary gliomas arise from these heterotopic glial nests.

Another rare instance of a myelinated ganglioneuroma of the cerebellar cortex was described by Alajouanine, Bertrand and Sabouraud.² The molecular layer was widened and myelinated while underneath it were many large neuroganglionic cells. Though considered a congenital malformation by the authors, clinically this lesion behaves like a growth. Two cases of neurogenic tumors involving the brain, both containing neuroblasts and ganglion cells, were reported by Hassin and Munch-Petersen.⁴⁷

Of a total of 157 surgically verified cases of glioblastoma multiforme, Davidoff and Feiring²⁷ observed 16 in which the tumor was a small, grossly circumscribed, reddish-gray, surface lesion often adherent to dura. In view of the size and location of these neoplasms, they appeared to be an ideal group for the purpose of testing the efficacy of treatment instituted early and radically. Treatment consisted of gross total removal followed by irradiation. The end results were no better than in the average case of glioblastoma multiforme. No patient lived longer than two years. Necropsy studies indicated that multiple centers of growth and the presence of tumor cells beyond the limits of excision accounted for the failure of treatment. A case of glioblastoma multiforme which metastasized to the lungs and kidney was reported by Brandt.¹⁴

Troland, Kendrick, Sahyoun and Mandeville⁹⁹ offered a classification of ependymomas as follows: Grade I, to include the papilloma choroideum, myxopapillary ependymoma and epithelial ependymoma; Grade II, the cellular form; Grade III, to include some of the malignant forms in which, together with the papillary and epithelial structures, are to be found syncytial areas, mitotic figures or oligodendroglia-like cells; Grade IV, "mantellomas," anaplastic tumors duplicating the cellular structure of the mantle layer and containing primitive neuroepithelial cells, spongioblasts, primitive pineal cells and medulloblasts. Malignant ependymomas which spread locally beyond the confines of the brain were reported by Feigin and Volk,³⁷ and by Meredith and Sahyoun.⁶⁷ The effect of ultrasound in ependymomas transplanted subcutaneously in C₃H mice was studied by

Brzustowicz, Herrick, Higgins, Bennett and Svien.¹⁶ While occasionally tumors a few millimeters in diameter were completely destroyed, in general, no inhibition of tumor growth was observed. An extraventricular, intracerebellar neoplasm possessing the structure of a papilloma of the choroid plexus was described by Greene.⁴⁵

An oligodendroglioma which metastasized extracranially, presumably the only instance of its kind in the literature, was described by James and Pagel.⁵³ Both the cerebral and extracranial lesions were studied by the Hortega method, which revealed argentaffine cells with fine polar processes. There was no evidence of reticulin formation by the tumor cells. Alajouanine, Bertrand, Castaigne and Blatrix¹ contributed a case report of an undifferentiated pinealoma which spread to involve the meninges and nerve roots.

Renard and David⁸² encountered the unusual phenomenon of a bilateral hyperostosing sphenoid wing meningioma.

Primary diffuse tumors of the meninges are rare. Black and Kernohan¹¹ found only four instances among 4500 neoplasms of the central nervous system studied at the Mayo Clinic. All four cases occurred in children or young adults. Two appeared to arise from meningotheial cells, one from fibroblasts and one from both meningotheial cells and fibroblasts.

The modes of spread of pituitary tumors beyond the limits of the sella turcica and their effects upon neighboring tissues were considered in detail by Trumble.¹⁰⁰ Downward growth into the sphenoidal sinus may result eventually in destruction of the floor of the sinus and protrusion into the nasopharynx. By extending through the roof of the sinus, the tumor may enter the anterior cranial fossa. Lateral spread compresses the cavernous sinus and the nerves contained therein. The tumor may continue to grow beneath the gasserian ganglion, surround the carotid artery and abducens nerve, enter the cavernous sinus and thereby extend through the superior orbital fissure into the orbit, along the superior petrosal sinus over the root of the trigeminal nerve, and along the inferior petrosal sinus beneath the dura of the floor of the posterior fossa. Upward escape of the neoplasm may occur through the opening in the diaphragma sella. Its relation henceforth to the optic pathways is most important. Usually the chiasm is pushed up and the tumor comes to lie in front of or behind it. A prefixed chiasm is displaced forward, a postfixed chiasm upward and backward. Eventually, the optic nerves, chiasm and tracts may be greatly stretched and elongated. The branches of the circle of Willis are intimately related to the expanding mass. The anterior cerebral arteries and the anterior communicating artery form an archway which stretches across the anterior aspect of the tumor. The posterior communicating arteries may be displaced laterally and the posterior cerebral and basilar arteries backwards. In time, the supracaloid

portion of the carotid artery may become entirely surrounded by tumor. Continued upward growth of the lesion will compress the hypothalamus, displace the chiasm forward, push the mamillary bodies backward against the peduncles, and thrust the optic tracts laterally against the medial surfaces of the temporal lobes. The anterior part of the third ventricle may become filled with tumor which may then gain access to the lateral ventricles by way of the foramen of Monro. As the growth fills the interpeduncular space, the midbrain becomes displaced posteriorly. Instead of rising upward behind the chiasm, the lesion may extend anteriorly between the optic nerves and continue upward and forward between the medial surfaces of the frontal lobes and backward toward the third ventricle. It may come to bear upon the parolfactory area overlying the head of the caudate nucleus and eventually involve the frontal horn of the lateral ventricle. Supradiaphragmatic extensions into the middle fossa compressing the temporal lobe may displace the basal ganglia, internal capsule and cerebral peduncle. Upward spread from the sella turcica may occur not only by way of the aperture in the diaphragm. A lateral expansion of the tumor may escape through the opening for the oculomotor nerve in the roof of the cavernous sinus. The surgical treatment of large pituitary tumors is also outlined. In approaching midline growths, a partial frontal lobectomy is advised. Should the tumor be placed behind the optic chiasm, the right anterior cerebral artery is ligated, the chiasm divided, and the third ventricle entered by way of the lamina terminalis and floor. Frontal and temporal extensions are approached through flaps in the corresponding regions.

Cerebral infarction due to tumor embolus was reported by Eason³³ in a case of primary carcinoma of the lung, the probable source being a pulmonary vein invaded by tumor. In 30 per cent of cases of metastatic tumor, Baker, Kernohan and Kiefer⁸ found single brain lesions. The lung was the primary site in 34 per cent of 100 cases studied at necropsy; the gastrointestinal tract accounted for 22 per cent, the breast 11 per cent, kidney 10 per cent and the skin (melanoma) 9 per cent. Shaw³⁰ described the rare occurrence of a Hürthle cell tumor of the thyroid which metastasized to the skull. Intracranial involvement by sarcoma botryoides, a mixed mesodermal tumor, of the uterus was reported by Friedland.⁴¹

Attention was drawn by Madow and Alpers⁶⁴ to an encephalitic form of metastatic carcinoma in which the lesions were diffusely scattered, infiltrating the parenchyma, perivascular spaces and meninges and unassociated with tumor formation. The incidence of this type of lesion is low, the authors having observed its occurrence in only four of 106 cases of metastatic disease. The primary site in three of the four cases was the lung; in one the primary site was undetermined. As might be expected, the clinical picture is not a distinctive one. All four patients showed evidence of

meningeal irritation, all had convulsions, three had an organic mental syndrome and three were hemiparetic. It is suggested that this condition be suspected in middle-aged or older patients with what appears to be an encephalitic process of undetermined origin.

Four instances of carcinomatosis of the leptomeninges were described by Jacobs and Richland.⁵¹ In one, the primary site was the stomach; in two, the primary source was not found at necropsy, but was presumed to be the gastro-intestinal tract. Based on their experiences and a study of the literature, the authors suggest that gastro-intestinal carcinoma spreading to intracranial structures tends to lodge in the leptomeninges rather than within nervous tissue (*sic*).

Intracranial extensions of tumors of the glomus jugularis were reported by Alexander, Beamer and Williams³ and by Dockerty, Love and Patton.³² The glomus jugularis consists of an aggregate of paraganglionic cells in the floor of the tympanic cavity just above the jugular bulb, within the temporal bone. Like the carotid body, it is composed to epithelioid elements in close juxtaposition to networks of fine vascular channels. The location, extent and vascularity of these intracranial extensions render surgical treatment exceedingly hazardous, and in the one case in which operation was attempted, a fatality resulted.

Two tumors of the nervous system, apparently of lymphatic origin, were encountered by Krayenbühl and Klinger.⁵⁹ One, a cavernous lymphangioma, involved the cauda equina; the other, a lymphangioendothelioma with lymphatic tissue, occurred close to the sagittal sinus.

Lipomas of the corpus callosum were discussed in two publications. Kinal, Rasmussen and Hamby⁶⁵ are of the opinion that surgical removal of these lesions is not feasible. Groff, Liu and Leopold,⁴⁶ on the other hand, believe that good results may be achieved through operation provided the third ventricle is not entered.

A case in which acromegaly and Cushing's syndrome coexisted was reported by McCormick, Reed, Murray and Ray.⁶⁵ An increased amount of adrenocorticotrophic hormone was demonstrated in the blood of the patient indicating that the acidophilic pituitary adenoma was the probable cause of the Cushing's syndrome and of the acromegaly. It would appear that adrenocorticotrophic hormone may be produced by the acidophilic cells of the pituitary and that hyperadrenalism and acromegaly may be caused by an acidophilic adenoma.

The successful transfer of human glioblastomas to the brains of rabbits, rats and guinea pigs was reported by Greene.⁴⁴ Attempts to transplant astrocytomas, ependymomas and a hemangioblastoma failed.

Further evidence to substantiate the hypothesis that spread of metastases from distant primary foci to the cerebrum may occur by way of the verte-

bral venous system, was presented by Anderson.⁴ By means of diodrast injections in cadavers and living patients, the segmental character of the vertebral venous system and its continuity with the cerebral venous sinuses was demonstrated. The ascending lumbar veins, the azygos venous system and deep cervical venous plexuses were shown to contribute to this network.

SYMPTOMATOLOGY AND DIAGNOSIS

A number of publications dealt with the use of radioactive substances for the localization of brain tumors. Further experience gained by Ashkenazy, Davis and Martin⁷ with radioactive diiodofluorescein confirmed their previous impressions regarding the value of this method. In a series of 340 cases suspected of neoplastic disease of the nervous system, there were only 17 proven errors. The results of the test were accurate in 90 per cent of a group of 150 histologically verified tumors; 17 grossly verified, but inoperable tumors, at or close to the midline were correctly diagnosed. The negative findings also proved to be 95 per cent correct. According to the authors, the extent of radioactive uptake by a tumor is dependent on its cellularity and vascularity. The more malignant the neoplasm, the greater the radiofluorescein concentration. There is little or no concentration of the dye over the site of chronic subdural hematomas and even less over large cysts. Metastatic carcinomas and sarcomas gave the highest differential counts, followed by the glioblastomas and vascular and cellular meningiomas. The astrocytomas and oligodendrogliomas gave the lowest differential counts. The uptake of dye by recurrent tumors is considerably greater owing to increased cellularity and vascularity. It is further indicated that the radiodye test does not distinguish between an acute infection and an anaplastic tumor since capillary permeability is disturbed in both instances. Special technics of counting have been evolved so that midline lesions may be localized with considerable accuracy. There appear to be no contraindications to this procedure. In another presentation, Davis²⁸ stated that aneurysms, arteriovenous fistulae and angiomas do not concentrate increased amounts of dye. Reference was also made to a new type of crystal probe counter devised to be used at the operating table in order to define the boundaries of an infiltrating glioma. Studies by Leroy, Tweedy and Ashkenazy⁶² of the distribution and excretion of radioactive diiodofluorescein would indicate that there is no significant radiation hazard associated with the amounts employed clinically.

Several papers were published by Moore and his co-workers^{21, 68, 69} at the University of Minnesota pertaining to the use of fluorescein, radioactive fluorescein, radioactive potassium and radioactive iodinated human serum albumin. The usefulness of the acid chromogen dye, sodium fluorescein, at the time of operation was again emphasized. This substance was also used

to demonstrate brain damage following the intraarterial injection of diodrast in rabbits. Some brains, on the side of the injection, revealed intense fluorescence indicating a breakdown of the blood brain barrier. Attempts to render brain tumors visible in the roentgenogram by the administration of various radio-opaque substances were unsuccessful. The use of radioactive diiodofluorescein for the detection of tumors proved feasible especially in the case of malignant tumors and those accompanied by edema. Growths less than three cm in diameter were often missed, and when situated in the posterior fossa or parasellar region, were difficult to find. The problem of detectors and methods of detector positioning were discussed. Adaptation of scintillation counters to clinical use should increase the validity of the radioactive dye test. The main route of excretion of radioactive diiodofluorescein was found to be by way of the bile. It was also indicated that with the use of purified, stable diiodofluorescein, there was little danger of I^{131} splitting off from the dye and being taken up by the thyroid gland. Moore and his group²¹ also reported on the use of radioactive iodinated human serum albumin as a tracer agent. This preparation has the advantage of being cheaper and staying in the tissues longer and permitting repeated counting. Moreover 400–500 μ c will give about the same counting rate as 1 mc of diiodofluorescein, and the differential uptake may be greater on the second or third day. Uptake of split off I^{131} by the thyroid may be prevented by the administration of Lugol's solution.

The use of radioactive potassium K^{42} for purposes of localization was studied by F. D. Moore and his associates⁹⁴ and by Selverstone, Sweet and Ireton.⁸⁹ Radioactive potassium emits a powerful gamma ray but its short half life makes its clinical use inconvenient. Both groups found it useful only in the localization of supratentorial tumors. The probe technic for demarcating cerebral neoplasms is less accurate with K^{42} since the beta radiation emitted possesses an energy more than twice that of P^{32} and increased counting may be obtained at some distance from the tumor.

Schlesinger⁸⁶ found that radioactive diiodofluorescein failed to afford localization in avascular tumors, lesions with fluid collections and vascular anomalies. This failure was thought to be due to the intrinsic vascular pattern of the lesion. Thoma and Woolsey⁹⁸ reported that in 24 patients with normal radiiodiodofluorescein records, no evidence of a tumor was revealed by other methods; the radioactive localization of the growth was verified in nine cases; six cases had been localized but not yet verified; in one the lesion was not localized, but found at operation. At the Mayo Clinic, Svien and Johnson⁹⁵ found that radioactive diiodofluorescein localized about 40 per cent of the gliomas of the cerebrum, convexity meningiomas, meningiomas of the lateral portion of the sphenoid ridge and metastatic tumors. Small, relatively acellular and deeply placed tumors

were difficult to localize satisfactorily. In contrast to the experience of most investigators, De Winter³¹ employing radioactive diiodofluorescein and a directional scintillation counter was able to localize the lesion in only one of 20 verified tumor cases.

In a consideration of the physical limitations of the diiodofluorescein method, Belcher and Evans⁹ indicated that it was possible to detect lesions concentrating I^{131} with the scintillation counter described, provided the concentration of activity in the lesion is ten times that of normal brain and the size of the lesion is greater than a certain minimum volume, depending on its depth. Thus, at a depth of 5 cm the limiting volume is 14 ml; at 8 cm this becomes 36 ml.

To minimize the factor of scattered gamma rays, Sweet⁹⁶ makes use of the special type of gamma rays emitted when a positron and an electron collide and are annihilated. These gamma rays go off in opposite directions and by means of a coincidence counting circuit only those pairs of gamma rays that are not scattered are registered. In the same article, Sweet also made reference to the use of energy developed as a result of nuclear disintegration to destroy neoplastic tissue. Boron¹⁰ which captures slow neutrons and then disintegrates can be sufficiently concentrated in brain tumors to suggest that irradiation with slow neutrons may be useful in their therapy.

Schütze and Klar⁸⁷ demonstrated fluorescence of brain tumors, employing atabrine as a fluorochrome vital stain.

In connection with the problem of using ultrasonic pulses to detect cerebral neoplasms, French, Wild and Neal⁴⁰ found no evidence of damage in animals when the brain was exposed to pulsed vibrations of 15 million cycles per second.

The signs and symptoms of 157 cases of acoustic neurofibroma were comprehensively reviewed by Edwards and Paterson.³⁵ Sixty-four per cent of patients were females, 36 per cent male. Over three-quarters of the patients began having symptoms between the ages of 30 and 60. Deafness or tinnitus were complained of in 92 per cent of cases and in 66 per cent cochlear symptoms constituted the initial manifestation. Tinnitus usually accompanied deafness (52 per cent). Vestibular symptoms occurred in 42 per cent of patients and were the initial complaint in 18 per cent. In ten patients, the vestibular symptoms were pronounced. Hearing on the side of the lesion was lost in 63 per cent and impaired in 36 per cent. Caloric responses were abolished in 83 per cent of cases tested and diminished in 15 per cent. Fifty-nine per cent of patients experienced trigeminal symptoms; 88 per cent had signs of trigeminal involvement, the corneal response being absent or defective in 87 per cent. Facial sensation was impaired in 62 per cent, while the motor component of the trigeminal nerve was affected in 20 per cent. Seven patients suffered tic-like pain, one on the side con-

tralateral to the tumor. Headache was complained of in 84 per cent of cases and was the initial symptom in 25 per cent. It was most commonly occipital or frontal in location. Twenty per cent of patients experienced suboccipital or neck pain. Cerebellar symptoms occurred in 77 per cent; ataxia of gait was observed in 79 per cent and incoordination of the limbs in 67 per cent. Nystagmus was present in 92 per cent of cases and, in about half of these, it was both vertical and horizontal. The incidence of additional signs and symptoms was as follows: dysarthria, 12 per cent, diplopia, 38 per cent, abducens palsy, 20 per cent, facial palsy, 63 per cent, impaired taste, 77 per cent of cases tested, facial spasm, 11 per cent, pyramidal signs, 17 per cent and papilledema, 76 per cent. The cerebrospinal fluid pressure was above 170 mm of water in 75 per cent of cases tested, and the protein content higher than 70 mgm per cent in 97 per cent. In 12 patients, conjugate gaze was defective. Lower cranial nerve involvement occurred infrequently. Bilateral auditory, cerebellar and trigeminal signs were observed in 19 patients. The mean duration of symptoms was 3.6 years during half of which time only acoustic symptoms were noted. The mean order of onset of symptoms corresponded to that described by Cushing. Seven patients had bilateral acoustic neurofibromata and of these, there was evidence of neurofibromatosis in six. Neurofibromatosis occurred in only three of the 157 patients with unilateral tumors. The mean age of patients with unilateral tumors was 44.4 years; the corresponding age for the bilateral cases was 23.6 years.

According to Schlesinger,⁸⁵ "If a middle aged person or one past middle age develops mental changes, chiefly profound disturbances in memory and the abnormalities in behavior resulting therefrom, cerebrospinal fluid pleocytosis with or without xanthochromia and other abnormalities, signs of intracranial hypertension, and a series of pathological findings pointing toward midbrain, basal ganglia and cerebellum, in other words a disseminated localization, a glioma of the splenium of the corpus callosum should be considered the most likely clinical diagnosis." The incidence of findings in 20 cases, 17 gathered from the literature, and mostly glioblastoma multiforme was as follows: mental changes 100 per cent, sensory-motor signs 85 per cent, increased intracranial pressure 70 per cent, temporo-parieto-occipital signs 50 per cent, brain stem and cerebellar signs 45 per cent, basal ganglia signs 35 per cent, cerebrospinal fluid abnormalities, usually xanthochromia, pleocytosis and increased protein content 45 per cent.

A detailed study of tumors in the region of the tentorial opening was presented by Poursines and Paillas.⁷⁹ Chordomas, cholesteatomas and meningiomas may occur in this area. Anteriorly located tumors give rise early

in their course to cranial nerve palsies and evidence of compression of the peduncles. Intracranial hypertension is a late development. Tumors which are posteriorly placed, on the other hand, cause increased pressure at an early stage. Findings referable to the quadrigeminal plate and cerebellar signs may also be in evidence.

Madonick and Savitsky⁶³ found bloody or xanthochromic cerebrospinal fluid in five of six cases of melanoma of the brain, the diagnosis being confirmed at autopsy in three cases and at operation in one. They believe that subarachnoid hemorrhage occurs more frequently with melanoma than with other metastatic tumors of the brain. De Saussure, Scheibert and Hazouri³⁰ reported subarachnoid bleeding as the first manifestation in a patient with a frontal astrocytoma.

Brain tumors may at times simulate meningitis. Brown and Peyton¹⁵ collected three cases, a dermoid cyst of the frontal lobes, a bifrontal glioblastoma multiforme and a varix of the third ventricle, in which the presenting features were meningeal. In an atypical case of meningitis, the possibility of a tumor must be borne in mind.

The incidence of seizures in 102 patients with cerebral gliomas was reported to be 58 per cent by Daly, McCarty and Bickford.²⁶ The frequency of seizures could be directly correlated with the duration of symptoms, while an inverse relationship existed as regards histologic malignancy. All patients with olfactory or gustatory hallucinations, nine of ten patients with abdominal auras and ten of eleven patients with automatisms had temporal lobe tumors. Auras most often accompanied tumors of the temporal lobe, and were uncommon in tumors of the frontal lobe. Convulsions occurred in 28.5 per cent of 1182 cases of cerebral neoplasm analyzed by Bormann and Schiefer.¹³ The frequency of seizures in centroparietal tumors was 58 per cent; in temporal tumors it was 48 per cent and in frontal tumors 39 per cent. As regards type of tumor, the figures were as follows: oligodendroglioma, 64 per cent, astrocytoma, 59 per cent, ependymoma, 53 per cent, glioblastoma and meningioma, each 25 per cent. Focal seizures occurred most often in patients with neoplasms of the centroparietal region, while generalized convulsions were most common in cases of frontal lobe tumor. Auras were experienced in 23 per cent of cases with generalized convulsions; most often the tumor involved the temporal lobe.

Based on a review of 128 cases of intracranial neoplasms observed at the Ochsner Clinic, Soniat⁹¹ concluded that psychiatric symptoms are equally prominent in frontal and temporal lobe tumors. Slightly more than half of the entire series showed mental manifestations; this figure rose to about 75 per cent in patients with frontal and temporal lobe lesions. Spillane⁹² collected seven cases of Cushing's syndrome in four of which psychiatric

symptoms were present. A fifth case treated with irradiation to the pituitary region developed optic atrophy and dementia some three years after therapy; pneumoencephalography disclosed atrophy.

Another instance of polycythemia occurring in association with a cerebellar hemangioblastoma was reported by Woolsey.¹⁰¹ Cramer and Kimsey²⁴ found the incidence of polycythemia in cerebellar hemangioblastoma to be 9 per cent in preoperative cases and 64 per cent in recurrent cases.

Divergence paralysis was shown by Chamlin and Davidoff²⁰ to be an accompaniment of increased intracranial pressure not necessarily due to posterior fossa tumors. They observed this phenomenon in two more cases of supratentorial mass lesions. Ten cases of hyaline bodies in the optic discs were presented by Chambers and Walsh¹⁹ to illustrate the importance of this condition in neurologic diagnosis. In six of the cases, papilledema was suspected. Progressive loss of vision and central scotomas probably due to hyaline bodies were observed in one patient and progressive loss of visual fields in three others. Gogela and Rucker⁴² found changes in the visual fields usually considered psychogenic in 18 patients out of a total of 500 with frontal lobe tumors. In 15, the fields were contracted concentrically, in two, a spiral fatigue appeared, and in one a ring scotoma was demonstrable. The possible presence of an organic lesion must be considered even when psychogenic field defects are encountered.

Peabody and Olsen⁷⁵ gathered six cases in which diabetes insipidus existed in association with bronchogenic carcinoma. Since metastases were presumably responsible for the diabetes insipidus, it is suggested that whenever this symptom occurs, malignant disease be considered as an etiologic agent.

In an article on fibrous dysplasia of the skull, Feiring, Feiring and Davidoff³⁸ indicated that confusion may arise in distinguishing between this disease and the bony changes associated with meningioma. One of the most valuable differential criteria is the age of the patient. Fibrous dysplasia is a disorder of childhood and adolescence, whereas meningiomas, as a rule, occur during adult life. In three of the cases reported by the authors, a meningioma was suspected preoperatively. The involved sites in these cases were the orbital plate, sphenoid ridge and tuberculum sellae. Three cases of unilateral proptosis, also caused by fibrous dysplasia, were described by King and Hayes.⁵⁷ In two cases areas of decreased density were noted in the orbital roof.

The occurrence of brain tumors in patients with hyperostosis frontalis interna is purely fortuitous. Moore⁷⁰ found that the incidence of neoplastic disease in female hyperostotics was 6.22 per cent; in a control group the incidence was 6.14 per cent. For males, the corresponding values were 2.27 per cent and 7.86 per cent.

Cases were cited by Platt⁷⁸ in which it was possible to demonstrate ex-

foliated tumor cells in the ventricular, cisternal and spinal fluids as well as in cerebral cyst fluids. The presence of mononuclear type cells, other than lymphocytes, in these fluids should arouse suspicion of a neoplasm.

Two case presentations bear further testimony that neither encephalography nor angiography are infallible diagnostic procedures. Both tests disclosed no abnormality in a patient with an extensive glioblastoma multiforme, reported by Blackwood, Mosberg and Robinson.¹² King,⁵⁶ on the other hand, described a case of massive cerebral infarction due to thrombosis of the internal carotid artery in which the ventriculographic appearance was that of a space-occupying lesion.

Visualization of the intracranial venous system by means of diodrast injected through a catheter into the superior sagittal sinus or by retrograde flow into the superior bulb of the internal jugular vein was described by Ray, Dunbar and Dotter.⁸⁰ It is possible to demonstrate by this method partial or complete obstruction of the major venous sinuses. In the case of a tumor obstructing a sinus, such information is exceedingly important in guiding the surgeon faced with the problem of resecting the affected sinus.

TREATMENT: SURGICAL AND OTHERWISE

Total extirpation of acoustic neurinomas is urged by Bucy.¹⁷ In an article on surgical treatment, the operative technique is described in detail.

The results of third ventriculostomy in the treatment of obstructive internal hydrocephalus were considered in two papers. In a series of 17 cases including inoperable tumors of the third ventricle, thalamus, mid-brain and posterior fossa, stenosis of the aqueduct and an Arnold-Chiari malformation, Krayenbühl, Werner and Martin⁶⁰ reported lasting good results in ten cases and amelioration of symptoms for two and three years in two cases. The best results were obtained in cases of posterior third ventricle tumor. Scarff's⁸⁴ series consisted of 16 cases of aqueduct stenosis and 18 of neoplastic disease. Five patients died in the hospital, ten were temporarily helped and 19 permanently relieved. The operative hazards and end results were about the same in a comparable group of 20 cases in which a Torkildsen procedure was performed.

McKissock⁶⁶ prefers the transcortical approach in the treatment of colloid cyst of the third ventricle. The contents of the cyst are evacuated and its walls coagulated. Of 21 cases treated surgically, 15 survived. One patient subsequently died of a recurrence following reoperation.

A study of four patients with infiltrating tumors treated by means of cerebral hemispherectomy was presented by Crockett and Estridge.²⁵ All the patients died. The longest period of survival was four months; postmortem examination in this case disclosed a recurrence of the growth.

Jaeger⁵² reported two cases of parasagittal meningioma in which portions

of the superior longitudinal sinus were resected. In neither case had the sinus been completely occluded. The sinus, in one case, was resected between the rolandic vein and torcular Herophili. No cortical veins were ligated and the patient recovered. In the other case the sinus was resected at the site of entrance of the rolandic vein and a fatality ensued. Jaeger concluded that an unobstructed superior sagittal sinus may be interrupted surgically at any point provided patent rolandic veins are not ligated. The danger of air embolism in the course of removal of a meningioma arising along the superior longitudinal sinus was indicated in a report by Reichert.⁸¹ As prophylaxis against such an event, he suggested that the sinus be exposed through a trephine opening before the bone flap is reflected and that it be temporarily occluded by means of a rubber shod clamp until the removal of the tumor has been accomplished.

Several new surgical approaches were offered for consideration. Negrin⁷¹ recommended a posterior coronal incision and bilateral occipitoparietal bone flaps in the treatment of tumors of the pineal region. This would permit visualization of the area of pathology from both sides and might render the operation less hazardous. Ecker³⁴ proposed a lateral supratentorial approach to the cerebellopontine angle for acoustic nerve tumors. Through a posterior temporal craniotomy the temporal lobe is retracted, and a flap of tentorium reflected, exposing the surface of the tumor. Scoville and McLaurin⁸⁸ described a simplified approach to the pituitary region through a one and a half inch trephine opening placed well laterally and just above the orbital ridge.

Bilsland¹⁰ contributed a study of 63 cases in which hypotension was deliberately induced by arteriotomy during intracranial surgery. A blood pressure of less than 100 mm mercury was maintained for as long as six hours, the average time being three hours. The amount of blood withdrawn varied from 300 cc to 2600 cc. It was felt that the method was useful and warranted further trial. In reviewing the fatal cases in this series, the factor of hypotension appeared to play a major role in the outcome in only one case, that of an aneurysm in which the right anterior cerebral artery was clipped and the blood pressure maintained at a low level thereafter for 90 minutes. A large infarct was disclosed at necropsy, leading the author to conclude that the blood pressure should have been restored immediately after ligation.

The operative mortality in a series of 105 cases of chromophobe pituitary adenoma reported by Horrax⁴⁹ was 13.3 per cent. This figure fell to 3.9 per cent in the group of 76 patients without large intracranial extensions; it was 37.9 per cent in the 29 patients with large extrasellar components. A five-year follow-up of 58 cases revealed that five had died of recurrence. Twenty-seven patients treated by means of surgery alone have been fol-

lowed for two to 18 years. Of 24 patients in whom vision was improved, there has been no regression in 11 after five to 18 years and in eight after two to four years. Forty-six patients treated surgically and with irradiation have been followed for two to 18 years. In 18, visual improvement has been maintained for five to 16 years and in 16 from two to four years. Surgical treatment was necessary in 36 patients who failed to respond favorably to radiation therapy. Of 27 patients treated solely with irradiation, 16 were moderately or markedly improved. A trial of preliminary radiation is advocated in patients whose vision is not seriously impaired. Favorable results with radiotherapy in pituitary tumors were reported by den Hoed²⁹ and by Nittinger.⁷² The latter treated a group of 31 cases consisting of eight acromegalics, two patients with Cushing's syndrome and 21 with chromophobe tumors. Fifteen were improved and have remained well, 12 for periods of 5 to 13 years; the course of the disease was halted in six after repeated treatment; four improved but suffered recurrences subsequently; four were failures; two were improved but died of other causes. Ten cases of craniopharyngioma which appeared to have benefited from x-ray therapy were described by Leddy and Marshall.⁶¹

Radiation therapy in the treatment of brain tumors was discussed by Peirce and Bouchard.⁷⁶ The survival of patients with glioblastoma multiforme after operation and irradiation was 12 months or more in 47.9 per cent, 15 months or more in 29.1 per cent and 30 months or more in 8.3 per cent. The average survival of the known dead was 13.3 months. It is the authors' opinion that a tumor dose greater than 7500 r will be necessary to obtain further improvement. The survival of patients with astrocytoma after operation and irradiation was 12 months or more in 87.8 per cent, 24 months or more in 56.1 per cent, 48 months or more in 34 per cent and 96 months or more in 9.7 per cent. The average survival of those known to be dead was 33.9 months. It is anticipated that a tumor dose of 9000 r may prolong the period of useful survival of these patients. Radiation therapy is advised in cases of oligodendroglioma, ependymoma and medulloblastoma. In the treatment of meningioma, the results of x-ray therapy as an adjuvant to surgery have been encouraging.

A group of brain tumors in which postoperative roentgen treatment was administered, principally by a single protracted course of irradiation, was reviewed by Freid and Davidoff.³⁹ Exclusive of one case that lived over nine years, the average postoperative survival period of 30 cases of glioblastoma multiforme was 11.4 months. Survival was uninfluenced by the type of operation or the amount or method of irradiation. The average postoperative survival of 15 patients with cerebral astrocytoma was 29.7 months. The type of operation had little influence on the course of the disease. For most of the group, x-ray therapy was not followed by improve-

ment. The longer survivals appeared to be associated with the larger total doses of radiation. A better response to irradiation was observed in the group of six cerebellar astrocytomas and the survival period following operation was much longer. The average survival of six cases of medulloblastoma was 28.3 months, the longest survivals being associated with the larger roentgen dosages. Three cases of spongioblastoma polare, two cerebral and one pontine, were not affected by x-ray therapy. Three of four cases of cerebellar sarcoma appeared to be distinctly benefited.

A report by Erickson and Steelman³⁶ indicated that the administration of radioactive phosphorus to patients with glioblastoma multiforme did not increase their life expectancy.

REFERENCES

- ¹ Alajouanine, T., Bertrand, I., Castaigne, P., and Blatrix, C.: Pinéoloblastome avec envahissement méningé et radiculaire diffus. *Rev. neurol.* 83:268, 1950.
- ² Alajouanine, T., Bertrand, I., and Sabouraud, C.: Ganglioneurome myélinique diffus de l'écorce cérébelleuse. *Rev. neurol.* 84:3, 1951.
- ³ Alexander, E., Jr., Beamer, P. R., and Williams, J. O.: Tumor of the glomus jugulare with extension into the middle ear (nonchromaffin paraganglioma or carotid body type tumor). *J. Neurosurg.* 8:515, 1951.
- ⁴ Anderson, R.: Diodrast studies of the vertebral and cranial venous systems to show their probable role in cerebral metastases. *J. Neurosurg.* 8:411, 1951.
- ⁵ Arnstein, L. H., Boldrey, E., and Naffziger, H. C.: A case report and survey of brain tumors during the neonatal period. *J. Neurosurg.* 8:315, 1951.
- ⁶ Asenjo, A., Valladares, H., and Fierro, J.: Tuberculomas of the brain. *Arch. Neurol. & Psychiat.* 65:146, 1951.
- ⁷ Ashkenazy, M., Davis, L., and Martin, J.: An evaluation of the technic and results of the radioactive di-iodo-fluorescein test for the localization of intracranial lesions. *J. Neurosurg.* 8:300, 1951.
- ⁸ Baker, G. S., Kernohan, J. W., and Kiefer, E. J.: Metastatic tumors of the brain. *Surg. Clin. North Am.* August, 1951.
- ⁹ Belcher, E. H. and Evans, H. D.: The localization of cerebral tumours with radioactive derivatives of fluorescein. Physical limitations. *Brit. J. Radiol.* 24:272, 1951.
- ¹⁰ Bilsland, W. L.: Controlled hypotension by arteriotomy in intracranial surgery. *Anesthesia.* 6:20, 1951.
- ¹¹ Black, B. K. and Kernohan, J. W.: Primary diffuse tumors of the meninges (so called meningeal meningiomatosis). *Cancer.* 3:805, 1951.
- ¹² Blackwood, W., Mosberg, W. H., Jr., and Robinson, P. K.: Brain tumour with normal air encephalography and arteriography. *J. Neurosurg.* 8:322, 1951.
- ¹³ Bormann, H. and Schiefer, W.: Krampfanfälle bei Tumoren des Grosshirns. *Deutsche Ztschr. f. Nerven.* 166:1, 1951.
- ¹⁴ Brandt, M.: Zur Frage der Metastasierung der Gehirntumoren. *Arch. f. Psychiat.* 185:594, 1950.
- ¹⁵ Brown, I. A. and Peyton, W. T.: Brain tumors simulating meningitis. *J. Neurosurg.* 8:459, 1951.
- ¹⁶ Brzustowicz, R. J., Herrick, J. F., Higgins, G. M., Bennett, W. A., and Svien,

- H. J.: The effect of ultrasound upon transplanted ependymomas in C_3H mice. *Proc. Staff Meet., Mayo Clin.* 26:447, 1951.
- ¹⁷ Bucy, P. C.: Surgical treatment of acoustic tumors. *J. Neurosurg.* 8:547, 1951.
- ¹⁸ Cairns, H. and Mosberg, W. H., Jr.: Colloid cyst of the third ventricle. *Surg., Gynecol. & Obst.* 92:545, 1951.
- ¹⁹ Chambers, J. W. and Walsh, F. B.: Hyaline bodies in the optic discs: report of ten cases exemplifying importance in neurological diagnosis. *Brain.* 74:95, 1951.
- ²⁰ Chamlin, M. and Davidoff, L. M.: Divergence paralysis with increased intracranial pressure. *Arch. Ophthalmol.* 46:145, 1951.
- ²¹ Chou, S. N., Aust, J. B., Moore, G. E., and Peyton, W. T.: Radioactive iodinated human serum albumin as tracer agent for diagnosing and localizing intracranial lesions. *Proc. Soc. Exper. Biol. & Med.* 77:193, 1951.
- ²² Cooper, I. S. and Kernohan, J. W.: Heterotopic glial nests in the subarachnoid space: histopathologic characteristics, mode of origin and relation to meningeal gliomas. *J. Neuropath. & Exper. Neurol.* 10:16, 1951.
- ²³ —, Rynearson, E. H., MacCarty, C. S., and Power, M. H.: The catabolic effect of craniotomy and its investigative treatment with testosterone propionate. *J. Neurosurg.* 8:295, 1951.
- ²⁴ Cramer, F. and Kimsey, W.: Cerebellar hemangioblastomas. *Arch. Neurol. & Psychiat.* 65:649, 1951.
- ²⁵ Crockett, H. G. and Estridge, N. M.: Cerebral hemispherectomy. A clinical, surgical and pathologic study of four cases. *Bull. Los Angeles Neurol. Soc.* 16:71, 1951.
- ²⁶ Daly, D., MacCarty, C. S., and Bickford, R. G.: Seizures in patients with gliomas of the cerebral hemispheres. *Trans. Am. Neurol. A.* 159, 1950.
- ²⁷ Davidoff, L. M. and Feiring, E. H.: "Circumscribed" glioblastoma multiforme. *J. Neuropath. & Clin. Neurol.* 1:161, 1951.
- ²⁸ Davis, L.: The radioactive di-iodo-fluorescein test for the localization of intracranial lesions. *Ann. Roy. Coll. Surgeons England.* 9:349, 1951.
- ²⁹ den Hoed, D.: La radiothérapie des tumeurs cérébrales. *Acta radiol.* 34:309, 1950.
- ³⁰ De Saussure, R. L., Jr., Scheibert, C. D., and Hazouri, L. A.: Astrocytoma grade III associated with profuse subarachnoid bleeding as its first manifestation. *J. Neurosurg.* 8:236, 1951.
- ³¹ De Winter, J. G.: Some preliminary clinical observations on the use of radioactive isotopes for the localization of brain tumors. *Brit. J. Radiol.* 24:280, 1951.
- ³² Dockerty, M. B., Love, J. G., and Patton, M. B.: Nonchromaffin paraganglioma of the middle ear: report of a case in which the clinical aspects were those of a brain tumor. *Proc. Staff Meet., Mayo Clinic.* 26:25, 1951.
- ³³ Eason, E. H.: A case of cerebral infarction due to neoplastic embolism. *J. Path. & Bact.* 62:454, 1950.
- ³⁴ Ecker, A.: A lateral supratentorial approach to the cerebellopontine angle for acoustic nerve tumor. *Surgery.* 30:661, 1951.
- ³⁵ Edwards, C. H. and Paterson, J. H.: A review of the symptoms and signs of acoustic neurofibromata. *Brain.* 74:144, 1951.
- ³⁶ Erickson, T. C. and Steelman, H. F.: Clinical observations on patients with glioblastoma multiforme who have received radioactive phosphorus. *Arch. Neurol. & Psychiat.* 65:240, 1951.
- ³⁷ Feigin, I. and Volk, B. W.: Malignant ependymoma infiltrating the scalp. *Arch. Path.* 51:466, 1951.

- ³⁸ Feiring, W., Feiring, E. H., and Davidoff, L. M.: Fibrous dysplasia of the skull. *J. Neurosurg.* 8:377, 1951.
- ³⁹ Freid, J. R. and Davidoff, L. M.: Roentgen therapy of primary neoplasms of the brain. *Radiology.* 57:25, 1951.
- ⁴⁰ French, L. A., Wild, J. J., and Neal, D.: The experimental application of ultrasonics to the localization of brain tumors. *J. Neurosurg.* 8:198, 1951.
- ⁴¹ Friedland, L. M.: Intracranial metastasis of sarcoma botryoides. *Arch. Neurol. & Psychiat.* 66:491, 1951.
- ⁴² Gogela, L. J. and Rucker, C. W.: Psychogenic changes in the field of vision associated with tumors of the frontal lobe of the brain. *Am. J. Ophth.* 34:185, 1951.
- ⁴³ Grant, F. C. and Sayers, M. P.: Notes on a series of brain tumors. *J. Neurosurg.* 8:510, 1951.
- ⁴⁴ Greene, H. S. N.: The transplantation of tumors to the brains of heterologous species. *Cancer Research.* 2:529, 1951.
- ⁴⁵ Greene, R. C.: Extraventricular and intra-cerebellar papilloma of the choroid plexus. *J. Neuropath. & Exper. Neurol.* 10:204, 1951.
- ⁴⁶ Groff, R. A., Liu, C. T., and Leopold, R. L.: Lipoma of the corpus callosum: survey of the literature and report of two surgical cases. *Arch. Neurol. & Psychiat.* 65:253, 1951.
- ⁴⁷ Hassin, G. B. and Munch-Petersen, C. J.: Central neurogenic tumors (neuroblastoma and ganglioneuroma). *J. Neuropath. & Clin. Neurol.* 1:63, 1951.
- ⁴⁸ Hejtmancik, M. R., Bradfield, J. Y., Jr., and Herrmann, G. R.: Acromegaly and the heart: a clinical and pathologic study. *Ann. Int. Med.* 34:1445, 1951.
- ⁴⁹ Horrax, G.: The chromophobe pituitary adenomas: surgical and radiation treatment. *Surg. Clin. North Am.* 877, June, 1951.
- ⁵⁰ — and Wu, W. Q.: Postoperative survival of patients with intracranial oligodendroglioma with special reference to radical tumor removal. *J. Neurosurg.* 8:473, 1951.
- ⁵¹ Jacobs, L. L. and Richland, K. J.: Carcinomatosis of the leptomeninges. *Bull. Los Angeles Neurol. Soc.* 16:335, 1951.
- ⁵² Jaeger, R.: Observations on resection of the superior longitudinal sinus at and posterior to the rolandic venous inflow. *J. Neurosurg.* 8:103, 1951.
- ⁵³ James, T. G. I. and Pagel, W.: Oligodendroglioma with extracranial metastases. *Brit. J. Surg.* 39:56, 1951.
- ⁵⁴ Kelly, R.: Colloid cysts of the third ventricle. *Brain.* 74:23, 1951.
- ⁵⁵ Kinal, M. E., Rasmussen, G., and Hamby, W. B.: Lipoma of the corpus callosum. *J. Neuropath. & Clin. Neurol.* 1:168, 1951.
- ⁵⁶ King, A. B.: Massive cerebral infarction producing ventriculographic changes suggesting a brain tumor. *J. Neurosurg.* 8:536, 1951.
- ⁵⁷ King, R. B. and Hayes, G. J.: Unilateral proptosis due to fibrous dysplasia of bone. *Arch. Ophth.* 46:553, 1951.
- ⁵⁸ Klinger, M.: Über Knorpelgeschwülste der Schädelbasis mit intrakranieller Ausdehnung. *Acta Neurochir.* 1:337, 1951.
- ⁵⁹ Krayenbühl, H. and Klinger, M.: Lymphangiome im Nervensystem. *Confinia neurol.* 11:65, 1951.
- ⁶⁰ —, Werner, A., and Martin, F.: Le Traitement de l'hydrocéphalie interne occlusive (H.I.O.) par la ventriculostomie sus-optique. Résultats obtenus dans 17 cas. *Rev. neurol.* 83:256, 1950.
- ⁶¹ Leddy, E. T. and Marshall, T. M.: Roentgen therapy of pituitary adamantinomas (craniopharyngiomas). *Radiology.* 56:384, 1951.

- ⁶² LeRoy, G. V., Tweedy, W. R., and Ashkenazy, M.: Radioactive di-iodo¹³¹ fluorescein: the health physics aspects of its use for diagnostic studies. *J. Lab. & Clin. Med.* 37:122, 1951.
- ⁶³ Madonick, M. J. and Savitsky, N.: Subarachnoid hemorrhage in melanoma of the brain. *Arch. Neurol. & Psychiat.* 65:628, 1951.
- ⁶⁴ Madow, L. and Alpers, B. J.: Encephalitic form of metastatic carcinoma. *Arch. Neurol. & Psychiat.* 65:161, 1951.
- ⁶⁵ McCormick, R. V., Reed, C. E., Murray, R. H., and Ray, B. S.: Coexisting acromegaly and Cushing's syndrome. *Am. J. Med.* 10:662, 1951.
- ⁶⁶ McKissock, W.: The surgical treatment of colloid cyst of the third ventricle. *Brain.* 74:1, 1951.
- ⁶⁷ Meredith, J. M. and Sahyoun, P. F.: Ependymoblastoma grossly eroding and involving overlying dura and skull. *J. Neurosurg.* 8:214, 1951.
- ⁶⁸ Moore, G. E., Caudill, C. M., Marvin, J. F., Aust, J. B., Chou, S. N., and Smith, G. A.: Clinical and experimental studies of intracranial tumors with fluorescein dyes with an additional note concerning the possible use of K⁴² and Iodine¹³¹ tagged human albumin. *Am. J. Roentgenol.* 66:1, 1951.
- ⁶⁹ —, Kohl, D. A., Marvin, J. F., Wang, J. C., and Caudill, C. M.: Biophysical studies of methods utilizing fluorescein and its derivatives to diagnose brain tumors. *Radiology.* 55:344, 1950.
- ⁷⁰ Moore, S.: Morgani's syndrome and brain tumors. *J. Neurosurg.* 8:480, 1951.
- ⁷¹ Negrin, J.: A new approach in the surgical treatment of tumors in the pineal region. *Am. J. Surg.* 80:581, 1950.
- ⁷² Nittinger, D.: Ergebnisse der Strahlenbehandlung von Hypophysentumoren. *Strahlentherapie.* 82:367, 1950.
- ⁷³ Obrador, S. and Ley, E.: Personal experience with cerebral cysticercosis. *Acta Neurochir.* 1:434, 1951.
- ⁷⁴ Paschkis, K. E. and Cantarow, A.: Hypopituitarism: studies in pituitary tumors and Simmond's disease. *Ann. Int. Med.* 34:669, 1951.
- ⁷⁵ Peabody, H. D., Jr. and Olsen, A. M.: Association of bronchogenic carcinoma and diabetes insipidus: report of cases. *Proc. Staff Meet., Mayo Clinic.* 26:107, 1951.
- ⁷⁶ Peirce, C. B. and Bouchard, J.: Role of radiation therapy in control of malignant neoplasms of brain and brain stem. *Radiology.* 55:337, 1950.
- ⁷⁷ Petit-Dutaillis, D. and Daum, S.: Les méningiomes de la fossa postérieure. *Rev. neurol.* 83:241, 1950.
- ⁷⁸ Platt, W. R.: Exfoliative cell diagnosis of central nervous system lesions. *Arch. Neurol. & Psychiat.* 66:119, 1951.
- ⁷⁹ Poursines, Y. and Paillas, J. E.: Les chordomes sphéno-occipitaux et les tumeurs du foramen ovale. *Rev. d'oto-neuro-oph.* 23:65, 1951.
- ⁸⁰ Ray, B. S., Dunbar, H. S., and Dotter, C. T.: Dural sinus venography as an aid to diagnosis in intracranial disease. *J. Neurosurg.* 8:23, 1951.
- ⁸¹ Reichert, F. L.: The dangers of air embolism when removing meningiomas arising along the superior sagittal or longitudinal sinus. *J. Neurosurg.* 8:494, 1951.
- ⁸² Renard, G., and David, M.: Ostéome sphéno-temporo-orbitaire bilatéral avec méningiome en plaque. *Rev. neurol.* 83:387, 1950.
- ⁸³ Ringertz, N. and Nordenstam, H.: Cerebellar astrocytoma. *J. Neuropath. & Exper. Neurol.* 10:343, 1951.
- ⁸⁴ Scarff, J. E.: Treatment of obstructive hydrocephalus by puncture of the lamina terminalis and floor of the third ventricle. *J. Neurosurg.* 8:204, 1951.

- ⁸⁵ Schlesinger, B.: Gliomas involving the splenium of the corpus callosum. *Neurology*. 1:419, 1951.
- ⁸⁶ Schlesinger, E. B.: Experiences with the Moore technique of localization of cerebral tumors with radioactive substances. *Surg. Forum, Amer. Coll. Surg.*, 1950, Philadelphia, W. B. Saunders Co., 1951, p. 368.
- ⁸⁷ Schütze, R. and Klar, E.: Die vital Fluorochromierung von Hirntumoren mit Atebrin als diagnostisches Hilfsmittel bei Hirngeschwulstoperationen. *Der Chirurg*. 22:166, 1951.
- ⁸⁸ Scoville, W. B. and McLaurin, R.: Simplified approach to pituitary region by one and one half inch trephine. *Surgery*. 29:136, 1951.
- ⁸⁹ Selverstone, B., Sweet, W. H., and Ireton, R. J.: Radioactive potassium, a new isotope for brain tumor localization. *Surg. Forum, Amer. Coll. Surg.*, 1950, Philadelphia, W. B. Saunders Co., 1951, p. 371.
- ⁹⁰ Shaw, R. C.: Metastasizing goitre. Hürthle cell tumor of the thyroid and skull. *Brit. J. Surg*. 39:25, 1951.
- ⁹¹ Soniat, T. L. L.: Psychiatric symptoms associated with intracranial neoplasms. *Am. J. Psychiat.* 108:19, 1951.
- ⁹² Spillane, J. D.: Nervous and mental disorders in Cushing's syndrome. *Brain*. 74:72, 1951.
- ⁹³ Störtebecker, T. P.: Metastatic hypernephroma of the brain from a neurosurgical point of view. *J. Neurosurg*. 8:185, 1951.
- ⁹⁴ Susen, A. F., Small, W. T., and Moore, F. D.: Studies on the external diagnostic localization of brain lesions using radioactive potassium. *Surg. Forum, Amer. Coll. Surg.*, 1950, Philadelphia, W. B. Saunders Co., 1951, p. 362.
- ⁹⁵ Svien, H. J. and Johnson, A. B., II.: Fluorescein in the localization of brain tumors. *Proc. Staff Meet., Mayo Clinic*. 26:142, 1951.
- ⁹⁶ Sweet, W. H.: The uses of nuclear disintegration in the diagnosis and treatment of brain tumor. *New England. J. Med.* 245:875, 1951.
- ⁹⁷ Symposium on the results of operations on acoustic neuromas. *J. Neurol., Neurosurg. & Psychiat.* 13:268, 1950.
- ⁹⁸ Thoma, G. E. and Woolsey, R. D.: The localization of intracranial neoplasms with radioactive diiodofluorescein. *J. Lab. & Clin. Med.* 36:998, 1950.
- ⁹⁹ Troland, C. E., Kendrick, J. F., Sahyoun, P. F., and Mandeville, F. B.: Ependymoma: a critical re-evaluation of classification with report of cases. *J. Neuro-path. & Exper. Neurol.* 10:295, 1951.
- ¹⁰⁰ Trumble, H. C.: Pituitary tumours. Observations on large tumours which have spread widely beyond the confines of the sella turcica. *Brit. J. Surg*. 39:7, 1951.
- ¹⁰¹ Woolsey, R. D.: Hemangioblastoma of cerebellum with polycythemia. *J. Neurosurg*. 8:447, 1951.
- ¹⁰² Zülch, K. J.: Vorzugssitz, Erkrankungsalter und Geschlechtsbevorzugung bei Hirngeschwülsten als bisher ungeklärte Formen der Pathoklise. *Deutsche Ztschr. f. Nervenhe.* 166:91, 1951.

The Vascular System

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ANGIOGRAPHY

IN THE last two years the use of cerebral angiography has proved a most successful tool for the diagnosis of intracranial lesions. Neurologic surgeons, neurologists and radiologists have acquired such skill that percutaneous carotid angiography may be performed in 15 to 20 minutes in about 95 per cent of cases.^{13, 18, 20, 59} Ecker²⁴ described the technic in a monograph on the normal angiogram. Puncture of the vertebral artery is technically a more difficult procedure. Radner,⁷² in a small monograph, described vertebral angiography by means of catheterization of the radial artery. Under fluoroscopy, he was able to inject the artery in 70 per cent of 221 cases on the first attempt. Only four neurologic complications were encountered, of which two, in patients with previous brain stem softening, resulted fatally. Ray, Dunbar and Dotter,⁷³ have suggested that dural sinography, accomplished by means of a catheter introduced into the longitudinal sinus, might aid in the diagnosis of certain obscure cerebral conditions due to sinus or venous thrombosis.

The radiopaque media used for angiography have occasioned a great deal of discussion in the past year. Several new substances have caused an undue number of complications and have proved unsatisfactory for clinical use.^{10, 33} Some authors have emphasized the serious complications which have arisen due to diodrast angiography. In a series of 108 cases, Dunsmore et al.²² reported three deaths, four cases of permanent hemiplegia and seven transient complications. However, in the hands of most operators, the percentage of complications has not been more than three or four per cent—irrespective of the technic used (open or closed), or the media (diodrast or thorotrast).^{11, 18} The incidence of death following angiography has remained in general at 0.5 per cent or less. Usually the fatalities have been in patients suffering from severe neurologic disease and frequently in coma at the time of the procedure.^{11, 20, 24} It seems true as Dunsmore et al.²² suggested that the complications are more common in the elderly and arteriosclerotic patients. In fact, it would be surprising if, with the increased use of angiography for the diagnosis of cerebral hemorrhage and intra-

cranial aneurysms in seriously ill and comatose patients, the mortality rate did not increase.

The reactions to diodrast—thought originally to have been due to irritation of the vessel wall causing vasospasm—a condition which Ecker and Riemenschneider²⁵ have demonstrated, seem now to be due to alterations in the permeability of the vessels. Broman et al.,¹² showed in rabbits that repeated injection of 70 per cent diodrast regularly produced an alteration in the permeability of the vessel wall so that dyes, normally confined to the vascular system, passed through the blood-brain barrier. Bloor et al.¹⁰ confirmed these findings. Foltz et al.³¹ reported changes both in the permeability of the cerebral vessels and the electroencephalogram following the carotid injection of diodrast. Heimbürger and Freeman⁴⁶ also found changes in the electroencephalogram. Smith et al.⁸⁷ could not produce these changes in vascular permeability consistently after injection of 70 per cent diodrast, but only when certain batches, presumably those containing impurities, were used. They found three of five batches to produce changes in vascular permeability. Whether or not these pathologic alterations are due to impurities in some batches of diodrast remains to be demonstrated. Fortunately, the incidence of untoward reactions is relatively low.

In the past two years, minor modifications have been suggested in the operative²¹ and x-ray technic.^{77, 83} Cinematographic technics for taking continuous pictures during angiography do not appear to have been further developed. Sanchez-Perez and Carter,⁷⁹ have emphasized the need of more than the usual two to three roentgenograms after the injection of the dye.

ANATOMY

The normal anatomic arrangement of the cerebral blood vessels has been discussed in a number of publications in the past two years. Curry and Culbreth¹⁹ described the normal angiographic appearance of the cerebral vessels in a series of 50 normal angiograms. In his monograph on the subject, Ecker,²⁴ depicts not only the usual vascular arrangement, but the common anomalous vessels. In other reviews,^{13, 20} the anatomic relationship of the cerebral vessels as seen in angiography was also described. The distribution of the vessels supplied by the vertebral arteries was well outlined and illustrated by Radner.⁷² Torkildsen and Koppang⁹⁹ discussed the collateral circulation resulting when one carotid artery is occluded.

PHYSIOLOGY

During the past two years the normal and pathologic physiology of cerebral circulation has been studied extensively with the Kety-Schmidt blood flow technic. The subject is reviewed in the monograph of Schmidt.⁸² Heyman et al.,⁴⁸ found the cerebral blood flow in uremia to be moderately

decreased if generalized vascular disease were present but normal if vascular involvement were minimal. The cerebral oxygen consumption was reduced significantly in both circumstances although the total body metabolism was not measurably reduced. Henry et al.,⁴⁷ in studying cerebral circulation during gravitational stress, found consciousness to be lost when the mean cerebral blood pressure fell to 25 mm. of mercury. In conditions of temporary high acceleration, such as in a power dive, this limit might be exceeded without alterations in consciousness. Under such circumstances the cerebral venous oxygen saturation remained unchanged in spite of great falls in cerebral arterial pressure. It was assumed that consciousness was sustained because of the arteriovenous pressure differential. The effects of sympathectomy on the cerebral circulation of hypertensive individuals was investigated by Shenkin et al.⁸⁶ They found, using the nitrous oxide method, that sympathectomy for essential hypertension did not result in an altered cerebral blood flow. Since the arterial pressure was decreased, it would follow that the cerebral vascular resistance must also be decreased. This might explain the beneficial effects of the operation on cerebral symptoms. In hyperthyroidism, Scheinberg⁸¹ found no abnormality in the cerebral metabolic functions and could not relate psychic manifestations of hyperthyroidism to increased metabolism of the brain. The effects of head-up tilt on cerebral blood flow was studied by Hafkenschiel et al.⁴² who noted that sympathectomized patients had the same degree of incomplete vascular relaxation with the tilt as unoperated hypertensives. This failure of complete cerebral vasodilatation was considered as evidence of a circulating pressor substance in hypertensive individuals. In the psychoses of senility, Freyhan et al.³⁴ found, in general, a reduction in cerebral blood flow, cerebral oxygen consumption, oxygen content of cerebral venous blood and an increase in cerebral vascular resistance. Scheinberg⁸⁰ studied the effect upon the cerebral blood flow of stellate ganglion block for cerebral vascular disease in middle-aged individuals. The group of patients with no alteration in mental status had significantly lower cerebral blood flow, higher arteriovenous oxygen difference and higher cerebrovascular resistance than normal young people. The cerebral oxygen and cerebral glucose utilizations were normal. The group with abnormal mental status had lower cerebral oxygen tension, glucose utilization, blood flow and higher cerebrovascular resistance than a series of patients with normal mental status or a group of normal young subjects. Unilateral block of the stellate ganglion produced no change in cerebral metabolic functions in normal patients, those with hypertensive vascular disease or elderly patients with thrombosis. Shenkin et al.⁸⁵ studied the effects of bilateral stellate ganglionectomy on the circulation in seven patients. They found a significant decrease in the cerebral vascular resistance which was greatest

in those patients with the initially slowest blood flow and initially greatest cerebral vascular resistance. The effect of intracranial pressure on the cerebral blood flow was investigated by Ryder et al.⁷⁵ in experimental studies on monkeys. The arterial blood pressure and the cardiac output influenced both the cerebral blood flow and intracranial pressure.

In a well-written, lengthy discussion, Courville¹⁵⁻¹⁷ reviews the clinical and pathologic alterations resulting from cerebral anoxia. An excellent historical review of the subject is given and then a detailed description of the mechanism and nature of the structural alterations following anoxia in neonatal, infant and adult life. A much briefer review of the recent literature is given by Steegmann.⁸⁹ That the visual pathway fails quite early in anoxia is well known; Noell and Chinn⁶⁶ studied this phenomena in animals and concluded that the order of susceptibility was cerebral cortex, geniculate ganglion, retinal ganglion cells, bipolar cells and finally the photo-receptors.

VASCULAR ANOMALIES

Scalp. Amyes and Courville¹ discuss traumatic arteriovenous aneurysms of the scalp reviewing the literature and reporting one case. Rice-Oxley and Cooke⁷⁶ stated that temporal arteritis may be successfully treated by aureomycin.

Intracranial Aneurysms. Interest in intracranial aneurysms is increasing. The January, 1951 number of *The Journal of Neurosurgery* was devoted to a symposium on cerebral aneurysm and vascular abnormalities. Oscar Sugar⁹¹ emphasized the embryologic basis of aneurysms. Carmichael¹⁴ also discussed the pathogenesis of these vascular anomalies.

The clinical symptoms and signs of aneurysms within the head have been reviewed many times in the past two years.^{50, 51, 61, 63} The significance of spontaneous subarachnoid hemorrhage as an indication of an aneurysm is well appreciated. The more obscure manifestations such as optic nerve involvement⁵⁶ are perhaps less well known. Migraine may be the only manifestation of an intracranial aneurysm for years before its rupture.³² Roseman et al.⁷⁶ describe changes in the electroencephalograms of patients harboring intracranial aneurysms.

The treatment of intracranial aneurysm appears to have become more conservative recently with emphasis upon carotid ligation. The hemodynamic effect of the unilateral carotid ligation in man was discussed by Shenkin et al.⁸⁴ After ligation of the common carotid artery there was a marked increase in the cerebral vascular resistance. The cerebral blood flow was maintained at a normal level in three patients who had no clinical effects as the result of ligation. In one patient who became hemiplegic, the cerebral blood flow fell to an abnormally low level, the cerebral vascular

resistance was markedly increased and cerebral oxygen consumption markedly reduced. Apparently, the resistance across the circle of Willis was considerably increased after common carotid ligation. Pressure measurements in the occluded artery may prove the efficacy of the carotid ligation but its safety must be determined by the effects upon the cerebral blood flow. Poppen's⁷¹ experience with 143 surgically treated aneurysms within the intracranial cavity, led him to conclude that treatment should not be instigated until angiograms had been made on both sides to eliminate the possibility of a second asymptomatic aneurysm which might rupture later. He thought that the exposure of a large intracranial aneurysm directly attached to the circle of Willis was hazardous. In such cases ligation of the carotid artery was preferable. Voris¹⁰⁰ emphasized that in the patients over 50 years of age ligation of the carotid artery carried a high risk. In younger patients he stated that ligations should be done under local anesthesia with preliminary occlusion of the vessel for 20 to 30 minutes. If the intracarotid pressure above the occlusion was reduced to 30 per cent or less of the initial pressure or if the patient showed neurologic signs during the test period of occlusion only a partial ligation should be made initially. Later the vessel may be completely occluded. After ligation of the internal carotid, Voris advised repeated procaine blocks of the cervical sympathetic trunk on the side of the ligation and anticoagulant therapy for three or four days. Ecker and Riemenschneider²⁶ demonstrated that thrombosis may occur in an aneurysm after partial occlusion. That multiple cerebral aneurysms do occur and may be treated surgically was emphasized by Bassett⁴ in a case report of two aneurysms successfully trapped.

The treatment of spontaneous subarachnoid hemorrhage due to a ruptured aneurysm, demonstrated by angiography and not amenable to clipping, is agreed upon by most authors^{3, 28, 70, 104} who favor carotid ligation early because of the high mortality if a policy of watchful waiting is followed (table 1).

Arteriovenous Anomalies. The routine use of angiography in intracranial hemorrhage has demonstrated that angiomatous lesions of the brain are more common than previously suspected. The removal of these lesions surgically may be facilitated by the use of total spinal anesthesia or sympathetic blocking agents, both of which reduce the systemic blood pressure dramatically. Swanson et al.⁹⁴ stated that the removal of an angioma by block resection under such conditions is "technically a comparatively easy procedure." But most authors have operated without the benefit of this aid. Bassett,⁵ Pilcher et al.⁶⁹ and Sunder-Plassmann⁹² removed large angiomatous malformations successfully. Green et al.³⁸ ablated the occipital lobe to remove the cerebral angiomatous lesion associated with Sturge-Weber syndrome.

TRAUMATIC ARTERIOVENOUS ANEURYSMS

Traumatic carotid cavernous aneurysms are discussed by Mense.⁶² An arteriovenous aneurysm between the middle meningeal artery and the greater superficial petrosal sinus was reported by Fincher.³⁰ That subarachnoid hemorrhage may result from conditions other than aneurysm of the brain has been known for some time but is again emphasized by Madonick and Savitsky⁶⁰ and Echols and Rehfeldt²³ who present cases of cerebral tumor causing hemorrhage. Fincher²⁹ has called attention to subarachnoid hemorrhage as a symptom of intradural spinal tumor, and reported some five cases of cauda equina tumor associated with blood in the spinal fluid and, in some instances, choking of the optic disc. This enlight-

TABLE 1.—*Carotid Ligation for Intracranial Aneurysm*

Author	No. of Cases	Mortality		Hemiplegia
		Immediate	Late	
Bassett and Gass ³	22	1		1
Falconer ²⁸	50*	9		
Jaeger ⁶¹	6			2
Martin ⁶¹	110			6
Mount ⁶³	77†	9		
Poppen ⁷¹	101‡	3	8	7
Wechsler et al. ¹⁰⁴	30	3		2

* Includes some intracranial operations.

† Includes intracranial operations.

‡ In 40 intracranial operations, 8 deaths.

ening communication has broadened the concept of subarachnoid hemorrhage.

THROMBOSIS

Spontaneous Thrombosis of the Carotid Artery. Occlusion of the internal carotid artery in the neck has been more frequently recognized in the past few years. Although the symptomatology may be intermittent paresis and paresthesias, apoplectic-like histories are not uncommon. At times, the diagnosis may be made by palpating the solid artery in the neck¹⁰² but usually angiography or exposure of the vessel is necessary. Johnson and Walker⁵² reviewed the subject with emphasis on the angiographic findings. For treatment, Swanson⁹⁵ recommended excision of the artery but no treatment has been very effective.

Cerebral Thrombosis. Parkinson⁸⁸ admitted that the differential diagnosis

of cerebral accidents was difficult. Basilar artery thrombosis discussed by Gross et al.³⁹ and Biemond⁸ is a rare occurrence but its clinical picture is sufficiently distinctive that the diagnosis should be made.

Cerebral thrombosis is predisposed by circulatory insufficiency according to Wilson et al.¹⁰⁵ This is in keeping with the experimental studies of Thompson and Rhode⁹⁸ who found that neurologic sequelae following occlusion of the anterior cerebral artery in monkeys roughly paralleled the degree of peripheral hypotension. Berthrong and Sabiston⁷ also emphasized that the polycythemia of congenital heart disease predisposed to thrombosis of the cerebral vessels especially after operation. Such infarcted areas were prone to infection. Congenital heart disease, especially coarctation of the aorta, was not infrequently accompanied by cerebral aneurysms according to Berthrong and Sabiston.⁷

TABLE 2.—*Effect of Stellate Block on Cerebral Vascular Accidents*

Author	No. of Cases	Stellate Series		No. of Cases	Control Series	
		Mortality	Improvement		Mortality	Improvement
Amyes and Perry ²	44*		28			
Naffziger and Adams ⁶⁴	155		90			
Sussman et al. ⁹³	20	6		22	10	

* EEG improved in 5 of 7 cases.

Cerebral thrombosis may cause massive edema of the brain simulating brain tumor. King⁵³ reports such a case with angiographic findings.

Much has been written in the past two years on the treatment of cerebral thrombosis and embolism. The early suggestion of Leriche⁵⁵ that stellate block might improve the cerebral circulation following vascular accidents has been taken up again and in the past two years a number of papers have appeared on this subject. Naffziger and Adams⁶⁴ reported 155 cases of thrombosis, embolism, or vasospasm; 59 per cent of this group had good results with stellate block. Nielsen,⁶⁵ in the new edition of his textbook on clinical neurology, advised stellate block for the treatment of cerebral embolism and thrombosis. Nosik⁶⁷ also believed that stellate block is of value. Wilson et al.¹⁰⁵ have not been so impressed by its efficacy. Few series have been adequately controlled to demonstrate that there is a difference in the morbidity and mortality in patients treated and untreated by stellate block (table 2). Perhaps, the value of stellate block may be due partially to the fact that the systolic blood pressure is increased as the result of the block upon the cardiac output.

Furmanski³⁵ suggested that histamine or other vasodilator drugs might

be of value in increasing the cerebral circulation. Histamine phosphate given intravenously to initiate an immediate generalized vasodilatation was considered of particular value in those cases in which the actual site of the thrombosis was not known.

Sinus Thrombosis. Dural sinus thrombosis as a cause of pseudo-tumor cerebri was emphasized by Ray and Dunbar.⁷⁴ Hyland⁴⁹ reported two cases of sinus thrombosis complicating the puerperium. Thromboses of the cavernous sinus is usually the result of paranasal sinus infection according to Elfman²⁷ and Stuart et al.⁹⁰ The prognosis is much better since the introduction of chemotherapy and antibiotics. Lillie⁵⁷ reported only two deaths in 27 cases found in the literature of the past ten years.

HEMORRHAGE

That neurosurgical intervention in cerebral hemorrhage may be more effective than commonly supposed has been emphasized by several writers in the past year. Angiography allows an accurate localization of the clot according to Webster et al.¹⁰³ and often demonstrates the type of vascular abnormality. Grant and Austin³⁶ point out that intracerebral clots may be removed through a burr hole with gratifying results.

Pontine hemorrhage induces profound shock, collapse, unconsciousness and respiratory disturbances according to Steegmann⁸⁸ who analyzed a series of 17 cases.

The attempts to increase the cerebral circulation by anastomosis of the carotid artery to the jugular veins Beck et al.⁶ have in the past two years been pretty generally discredited. Experimentally, Gurdjian et al.⁴⁰ and Tarlov et al.⁹⁶ showed that in monkeys such an anastomosis did not produce an increase in the amount of blood entering the cerebral hemispheres, but that the blood entering the cranium passed across the torcular herophili to the opposite lateral sinus and out the jugular vein. In man, this shunt could be demonstrated in many, although not all, cases. Moreover, Gurdjian et al.⁴¹ did not find the oxygen tension of the blood in the longitudinal sinus increased after the operation. In the clinical evaluation of a series of cerebral palsied patients by Hammer et al.,⁴³ only one of 33 patients was judged improved.

VASCULAR TUMORS

Vascular tumors of the spinal cord^{54, 58, 97} and brain continue to be pathologic curiosities. The cerebellar hemangioblastomas, Woolsey¹⁰⁶ states, are prone to be associated with polycythemia, which disappears when the tumor is removed. These tumors, according to Grant and Sayers²⁷ have "the most hopeful record of any intracranial lesion."

REFERENCES

- ¹ Amyes, E. W. and Courville, C. B.: Traumatic arteriovenous aneurysm of the scalp; review of literature and report of case. *Bull. Los Angeles Neurol. Soc.* 15:47-58, 1950.
- ² — and Perry, S. M.: Stellate ganglion block in the treatment of acute cerebral thrombosis and embolism. *J.A.M.A.* 142:15-20, 1950.
- ³ Bassett, R. C. and Gass, H. H.: Ligation of internal carotid artery for aneurysmal lesions of circle of Willis. *J.A.M.A.* 147:842-846, 1951.
- ⁴ Bassett, R. C.: Multiple cerebral aneurysms. *J. Neurosurg.* 8:132-133, 1951.
- ⁵ —: Surgical experiences with arteriovenous anomalies of the brain. *J. Neurosurg.* 8:59-74, 1951.
- ⁶ Beck, C. S., McKhann, C. F., and Belnap, W. D.: Revascularization of brain through establishment of cervical arteriovenous fistula; effects in children with mental retardation and convulsive disorders. *J. Pediat.* 35:317-329, 1949.
- ⁷ Berthrong, M. and Sabiston, D. C., Jr.: Cerebral lesions in congenital heart disease. A review of autopsies on one hundred and sixty-two cases. *Bull. Johns Hopkins Hosp.* 89:384-406, 1951.
- ⁸ Biemond, A.: Thrombosis of the basilar artery and the vascularization of the brain stem. *Brain.* 74:300-317, 1951.
- ⁹ Bloor, B. M., Wrenn, F. R., Jr., and Hayes, G. J.: An experimental method for the evaluation of contrast media used in cerebral angiography. *J. Neurosurg.* 8:435-440, 1951.
- ¹⁰ —, Wrenn, F. R., Jr., and Margolis, G.: An experimental evaluation of certain contrast media used for cerebral angiography. *J. Neurosurg.* 8:585-594, 1951.
- ¹¹ Boldrey, E., Miller, E. R., and Kendrick, J.: Clinical difficulties encountered in cranial angiography. Presented at the Am. Acad. Neurol. Surg. October 4, 1951.
- ¹² Broman, T., Forssman, B., and Olsson, O.: Further experimental investigations of injuries from contrast media in cerebral angiography. Summation of various injurious factors. *Acta Radiol.* 34:135-143, 1950.
- ¹³ Cairns, H. and Jupe, M. H.: *A Textbook of X-Ray Diagnosis by British Authors.* Edited by S. C. Shanks and P. Kerley. 2nd Ed. Philadelphia and London, W. B. Saunders Co., 1951. (Volume I, Chapter 4.)
- ¹⁴ Carmichael, R.: Pathogenesis of non-inflammatory cerebral aneurysms. *J. Path. & Bact.* 62:1-19, 1950.
- ¹⁵ Courville, C. B.: Contributions to the study of cerebral anoxia. I. Asphyxia in legend, folklore, and history. *Bull. Los Angeles Neurol. Soc.* 15:99-128, 1950.
- ¹⁶ —: Contributions to the study of cerebral anoxia. II. The mechanism and nature of consequent structural alterations. *Bull. Los Angeles Neurol. Soc.* 15:129-154, 1950.
- ¹⁷ —: Contributions to the study of cerebral anoxia. III. Neonatal asphyxia and its relation to certain degenerative diseases of the brain in infancy and childhood. *Bull. Los Angeles Neurol. Soc.* 15:155-195, 1950.
- ¹⁸ Culbreth, G. G., Walker, A. E., and Curry, R. W.: Cerebral angiography in brain tumor suspects. *J. Neurosurg.* 7:127-138, 1950.
- ¹⁹ Curry, R. W. and Culbreth, G. G.: The normal cerebral angiogram. *Am. J. Roentgenol.* 65:345-373, 1951.
- ²⁰ Curtis, J. B.: Cerebral angiography. *Brit. J. Surg.* 38:295-331, 1951.
- ²¹ Drake, C. G.: Arteriography. *J. Neurosurg.* 8:545-546, 1951.
- ²² Dunsmore, R., Scoville, W. B., and Whitcomb, B. B.: Complications of angiography. *J. Neurosurg.* 8:110-118, 1951.

- ²³ Echols, D. H. and Rehfeldt, F. C.: Profuse subarachnoid hemorrhage caused by cerebral glioma. *J. Neurosurg.* 7:280-282, 1950.
- ²⁴ Ecker, A.: *The Normal Cerebral Angiogram*. Springfield, Ill., Charles C Thomas, 1951.
- ²⁵ — and Riemenschneider, P. A.: Arteriographic demonstration of spasm of the intracranial arteries. *J. Neurosurg.* 8:660-667, 1951.
- ²⁶ —: Deliberate thrombosis of intracranial arterial aneurysm by partial occlusion of the carotid artery with arteriographic control. Preliminary report of a case. *J. Neurosurg.* 8:348-353, 1951.
- ²⁷ Elfman, L. K.: Thrombosis of cavernous sinus: New evaluation and report of case with recovery. *Arch. Otolaryng.* 51:188-195, 1950.
- ²⁸ Falconer, M. A.: The surgical treatment of bleeding intracranial aneurysms. *J. Neurol., Neurosurg. & Psychiat.* 14:153-186, 1951.
- ²⁹ Fincher, E. F.: Spontaneous subarachnoid hemorrhage in intradural tumors of the lumbar sac. *J. Neurosurg.* 8:576-584, 1951.
- ³⁰ —: Arteriovenous fistula between the middle meningeal artery and the greater petrosal sinus: Case report. *Ann. Surg.* 133:886-888, 1951.
- ³¹ Foltz, E. L., Thomas, L. B., and Ward, A. A., Jr.: The effects of intracarotid diodrast. *J. Neurosurg.* 9:68-82, 1952.
- ³² Frankel, K.: Relation of migraine to cerebral aneurysm. *Arch. Neurol. & Psychiat.* 63:195-204, 1950.
- ³³ French, L. A. and Blake, P. S.: Complications following the use of neo-iopex in cerebral angiography. *Am. J. Roentgenol.* 64:816-818, 1950.
- ³⁴ Freyhan, F. A., Woodford, R. B., and Kety, S. S.: Cerebral blood flow and metabolism in psychoses of senility. *J. Nerv. & Ment. Dis.* 113:449-456, 1951.
- ³⁵ Furmanski, A. R.: Histamine therapy in acute ischemia of brain. *Arch. Neurol. & Psychiat.* 63:415-424, 1950.
- ³⁶ Grant, F. C. and Austin, G. M.: Surgical treatment of spontaneous and traumatic intracerebral hemorrhage. *Am. J. M. Sc.* 219:237-241, 1950.
- ³⁷ — and Sayers, M. P.: Notes on a series of brain tumors. *J. Neurosurg.* 8:510-514, 1951.
- ³⁸ Green, J. R., Foster, J., and Berens, D. L.: Encephalotrigeminal angiomatosis (Sturge-Weber Syndrome) with particular reference to roentgenological aspects before and after neurosurgery. *Am. J. Roentgenol.* 64:391-397, 1950.
- ³⁹ Gross, S. W., Lisa, J. R., and Soffer, L. J.: Thrombosis of the basilar artery. *Arch. Neurol. & Psychiat.* 66:223-226, 1951.
- ⁴⁰ Gurdjian, E. S., Webster, J. E., and Martin, F. A.: Carotid-internal jugular anastomosis in rhesus monkey: Angiographic and gasometric studies. *J. Neurosurg.* 7:467-472, 1950.
- ⁴¹ —: Vasometric studies in carotid-internal jugular anastomosis in the neck. *Arch. Surg.* 63:466-476, 1951.
- ⁴² Hafkenschiel, J. H., Crumpton, C. W., Shenkin, H. A., Moyer, J. H., Zintel, H. A., Wendel, H., and Jeffers, W. A.: The effects of twenty degree head-up tilt upon the cerebral circulation of patients with arterial hypertension before and after sympathectomy. *J. Clin. Investigation.* 30:793-798, 1951.
- ⁴³ Hammer, J. M., Heersma, H. S., MacGregor, J. R., Dew, R. S., and Osius, E. A.: Complications and effects observed in 33 patients with cervical arteriovenous fistulas. *Arch. Surg.* 63:477-479, 1951.
- ⁴⁴ Harvey, J. and Rasmussen, T.: Electroencephalographic changes associated with

- experimental temporary focal cerebral anemia. *EEG Clin. Neurophysiol.* 3:341-351, 1951.
- ⁴⁵ —: Occlusion of middle cerebral artery; an experimental study. *Arch. Neurol. & Psychiat.* 66:20-29, 1951.
 - ⁴⁶ Heimburger, R. and Freeman, W. L.: Electroencephalography during angiography. Presented at the Harvey Cushing Society, 26 April 1951.
 - ⁴⁷ Henry, J. P., Gauer, O. H., Kety, S. S., and Kramer, K.: Factors maintaining cerebral circulation during gravitational stress. *J. Clin. Investigation.* 30:292-300, 1951.
 - ⁴⁸ Heyman, A., Patterson, J. L., Jr., and Jones, R. W., Jr.: Cerebral circulation and metabolism in uremia. *Circulation.* 3:558-563, 1951.
 - ⁴⁹ Hyland, H. H.: Intracranial venous thrombosis in the puerperium. *J.A.M.A.* 142:707-710, 1950.
 - ⁵⁰ —: Prognosis in spontaneous subarachnoid hemorrhage. *Arch. Neurol. & Psychiat.* 63:61-78, 1950.
 - ⁵¹ Jaeger, R.: Aneurysm of the intracranial carotid artery. Syndrome of frontal headache with oculomotor nerve paralysis. *J.A.M.A.* 142:304-310, 1950.
 - ⁵² Johnson, H. C. and Walker, A. E.: The angiographic diagnosis of spontaneous thrombosis of the internal and common carotid arteries. *J. Neurosurg.* 8:631-659, 1951.
 - ⁵³ King, A. B.: Massive cerebral infarction producing ventriculographic changes suggesting a brain tumor. *J. Neurosurg.* 8:536-539, 1951.
 - ⁵⁴ Lam, R. L., Roulhac, G. E., and Erwin, H. J.: Hemangioma of the spinal canal and pregnancy. *J. Neurosurg.* 8:668-671, 1951.
 - ⁵⁵ Leriche, R. and Fontaine, R.: De l'infiltration stellaire dans les embolies cérébrales dans les spasmes vasculaires postopératoires de l'encephale et chez les hémiplegiques. *Rev. de chir.* 74:755-758, 1936.
 - ⁵⁶ Ley, A.: Compression of optic nerve by fusiform aneurysm of carotid artery. *J. Neurol., Neurosurg. & Psychiat.* 13:75-86, 1950.
 - ⁵⁷ Lillie, H. I.: Prognosis of septic thrombophlebitis of the cavernous sinus. *J. Internat. Coll. Surgeons.* 15:754-759, 1951.
 - ⁵⁸ Lindstrom, P. A.: Primary extradural spinal hemangiomas. *Bull. Los Angeles Neurol. Soc.* 16:202-208, 1951.
 - ⁵⁹ List, C. F.: Cerebral angiography. *Radiology.* 55:327-329, 1950.
 - ⁶⁰ Madonick, M. J. and Savitsky, N.: Subarachnoid hemorrhage in melanoma of the brain. *Arch. Neurol. & Psychiat.* 65:628-636, 1951.
 - ⁶¹ Martin, J.: The diagnosis and surgical treatment of intracranial aneurysms. *Am. Surgeon.* 17:853-858, 1951.
 - ⁶² Mense, J. S.: Carotid-cavernous communications; a study of its causative mechanism and resultant angiographic patterns in the light of three personally observed cases. *Bull. Los Angeles Neurol. Soc.* 16:88-108, 1951.
 - ⁶³ Mount, L. A.: Treatment of spontaneous subarachnoid hemorrhage. *J.A.M.A.* 146:693-698, 1951.
 - ⁶⁴ Naffziger, H. C. and Adams, J. E.: Role of stellate block in various intracranial pathologic states. *Arch. Surg.* 61:286-293, 1950.
 - ⁶⁵ Nielsen, J. M.: A Textbook of Clinical Neurology. New York, P. B. Hoeber, 1951, 3rd ed.
 - ⁶⁶ Noell, W. and Chinn, H. I.: Failure of visual pathway during anoxia. *Am. J. Physiol.* 161:573-590, 1950.

- ⁶⁷ Nosik, W. A.: Stellate ganglion block in cerebrovascular accidents. *Ann. Int. Med.* 35:409-416, 1951.
- ⁶⁸ Parkinson, D.: Cerebral vascular accidents. *Canad. M. A. J.* 64:436-439, 1951.
- ⁶⁹ Pilcher, C., Meacham, W. F., and Cobb, C. A.: The surgical treatment of intracranial angiomatous malformations. *Surgery.* 28:342-349, 1950.
- ⁷⁰ Poppen, J. L.: Ligation of internal carotid artery in neck: Prevention of certain complications. *J. Neurosurg.* 7:532-538, 1950.
- ⁷¹ —: Specific treatment of intracranial aneurysms: Experiences with 143 surgically treated patients. *J. Neurosurg.* 8:75-102, 1951.
- ⁷² Radner, S.: Vertebral angiography by catheterization; a new method employed in 221 cases. *Acta Radiol. Suppl.* 87, pp. 1-134, 1951.
- ⁷³ Ray, B. S., Dunbar, H. S., and Dotter, C. T.: Dural sinus venography as an aid to diagnosis in intracranial disease. *J. Neurosurg.* 8:23-37, 1951.
- ⁷⁴ — and Dunbar, H. S.: Thrombosis of the dural venous sinuses as a cause of "pseudo tumor cerebri." *Ann. Surg.* 134:376-386, 1951.
- ⁷⁵ Rice-Oxley, J. M. and Cooke, A. M.: Temporal arteritis: Two cases treated with aureomycin. *Lancet.* 260:89-90, 1951.
- ⁷⁶ Roseman, E., Bloor, B. M., and Schmidt, R. P.: The electroencephalogram in intracranial aneurysms. *Neurology.* 1:25-38, 1951.
- ⁷⁷ Rosenberg, L. S. and Simpson, J. R.: A simple serialographic technic for cerebral angiography. *Radiology.* 54:869-874, 1950.
- ⁷⁸ Ryder, H. W., Epsey, F. F., Kristoff, F. V., and Evans, J. P.: Observations on the interrelationships of intracranial pressure and cerebral blood flow. *J. Neurosurg.* 8:46-58, 1951.
- ⁷⁹ Sanchez-Perez, J. M. and Carter, R. A.: Time factor in cerebral angiography and automatic seriograph. *Am. J. Roentgenol.* 62:509-518, 1949.
- ⁸⁰ Scheinberg, P.: Cerebral blood flow in vascular disease of brain with observations on effects of stellate ganglion block. *Am. J. Med.* 8:139-147, 1950.
- ⁸¹ —: Cerebral circulation and metabolism in hyperthyroidism. *J. Clin. Investigation.* 29:1010-1013, 1950.
- ⁸² Schmidt, C. F.: *The Cerebral Circulation in Health and Disease.* Springfield, Ill., Charles C Thomas, 1950.
- ⁸³ Scott, W. G. and Seaman, W. B.: Developments in cerebral angiography with rapid serialized x-ray exposures on roll film 9½ inches wide. *Radiology.* 56:15-30, 1951.
- ⁸⁴ Shenkin, H. A., Cabieses, F., van den Noordt, G., Sayers, P., and Cooperman, R.: The hemodynamic effect of unilateral carotid ligation on the cerebral circulation of man. *J. Neurosurg.* 8:38-45, 1951.
- ⁸⁵ —, Cabieses, F. and van den Noordt, G.: Effect of bilateral stelletomy upon the cerebral circulation of man. *J. Clin. Investigation.* 30:90-93, 1951.
- ⁸⁶ —, Hafkenschiel, J. H., and Kety, S. S.: Effects of sympathectomy on the cerebral circulation of hypertensive patients. *Arch. Surg.* 61:319-324, 1950.
- ⁸⁷ Smith, G. A., Caudill, C. M., Moore, G. E., Peyton, W. T., and French, L. A.: Experimental evaluation of cerebral angiography. *J. Neurosurg.* 8:556-563, 1951.
- ⁸⁸ Stegmann, A. T.: Primary pontile hemorrhage; with particular reference to respiratory failure. *J. Nerv. & Ment. Dis.* 114:35-65, 1951.
- ⁸⁹ —: Clinical aspects of cerebral anoxia in man. *Neurology.* 1:261-274, 1951.
- ⁹⁰ Stuart, E. A., O'Brien, F. H., and McNally, W. J.: Cerebral venous thrombosis: Its occurrence: Its localization: Its sources and sequelae. *Ann. Otol., Rhin. & Laryng.* 60:406-438, 1951.

- ⁹¹ Sugar, O.: Pathological anatomy and angiography of intracranial vascular anomalies. *J. Neurosurg.* 8:3-22, 1951.
- ⁹² Sunder-Plassmann, P.: Die operative Behandlung (Hirnlappenresektion) ausgedehnter arterio-venöser Aneurysmen des Gehirns. *Deutsche med. Wchnschr.* 75:163-166, 1950.
- ⁹³ Sussman, I., Lempke, R., and Wallace, R.: Stellate ganglion block in cerebral thrombosis and embolism: A preliminary report. *Am. Pract.* 2:217-220, 1951.
- ⁹⁴ Swanson, H. S., Galvin, W. H., and Fincher, E. F.: Total spinal anesthesia in the surgical management of a congenital arteriovenous aneurysm. *Surg., Gynec. & Obst.* 93:215-220, 1951.
- ⁹⁵ —: Spontaneous thrombosis of the internal carotid artery. *South. M. J.* 44:705-711, 1951.
- ⁹⁶ Tarlov, I. M., Shure, B., Epstein, B. S., Hirsch, E., and Nissen, R.: Brain revascularization after carotid-jugular anastomosis assessed by angiography. *Arch. Neurol. & Psychiat.* 64:847-860, 1950.
- ⁹⁷ Taylor, J., Harries, B. J., and Schurr, P. H.: Extrathecal hemangiolipomas of the spinal cord. *Brit. J. Surg.* 39:1-7, 1951.
- ⁹⁸ Thompson, R. K. and Rhode, C. M.: Effects of anterior cerebral circulation occlusion with varying levels of blood pressure in the Macaque. *J. Nerv. & Ment. Dis.* 112:58-65, 1950.
- ⁹⁹ Torkildsen, A. and Koppang, K.: Notes on the collateral cerebral circulation as demonstrated by carotid angiography. *J. Neurosurg.* 8:269-278, 1951.
- ¹⁰⁰ Voris, H. C.: Complications of ligation of the internal carotid artery. *J. Neurosurg.* 8:119-131, 1951.
- ¹⁰¹ Waters, R. A. and McCravey, A.: Non-traumatic intracranial hemorrhage. *J. Tennessee M. A.* 43:243-245, 1950.
- ¹⁰² Webster, J. E., Dolgoff, S., and Gurdjian, E. S.: Spontaneous thrombosis of carotid arteries in neck: Report of 4 cases. *Arch. Neurol. & Psychiat.* 63:942-953, 1950.
- ¹⁰³ —, Dawson, R., and Gurdjian, E. S.: The diagnosis of traumatic intracranial hemorrhage by angiography. *J. Neurosurg.* 8:368-376, 1951.
- ¹⁰⁴ Wechsler, I. S., Gross, S. W., and Cohen, I.: Arteriography and carotid artery ligation in intracranial aneurysm and vascular malformation. *J. Neurol., Neurosurg. & Psychiat.* 14:25-34, 1951.
- ¹⁰⁵ Wilson, G., Rupp, C., Jr., Riggs, H. E., and Wilson, W. W.: Factors influencing the development of cerebral vascular accidents. I. Role of cardiocirculatory insufficiency. *J.A.M.A.* 145:1227-1229, 1951.
- ¹⁰⁶ Woolsey, R. D.: Hemangioblastoma of the cerebellum with polycythemia. Case report. *J. Neurosurg.* 8:447-450, 1951.

Psychosurgery

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LICEITY and deontology are two words that have recently arisen in connection with surgery for the relief of mental disorders. Some psychiatrists feel that operations on anatomically normal brains of sufferers from functional mental disorders are offensive, morally wrong. This attitude is supported by gloomy word pictures of the devastating effects of lobotomy upon personality. Psychiatrists working in mental hospitals see the surgeons' failures. Baruk³ is especially bitter in condemnation: "As for the schizophrenics treated by this method, those that I've seen were almost always terribly worse; to the dynamic aberration of the schizophrenia there was added a dementing organic affliction with weakening of memory, carelessness and regression." Prick⁴² stresses the reduction in fantasy and in dream life of his patients, finding disturbance in the cognitive faculty, weakened sensitivity and decrease in self-determination or will. These alterations occurred in five psychasthenics that were followed for three years after lobotomy limited to one side. He concluded that there was extensive deterioration and regression to primitive behavior; "Therefore the illusory affective improvement. . . their recognition of God and their orientation toward His will have withdrawn into the fine points of the soul."

It is difficult to harmonize these viewpoints with those of Worthing:⁶¹ "Perhaps the most feared and most discussed complication of prefrontal lobotomy is the so-called 'personality change.' Our experience leads us to the opinion that the present status of this problem is somewhat analogous to that of the vertebral fracture issue as it stood some ten years ago. In this series, personality change, or loss, or disinhibition has been no problem, in the hospital or out. Complaints have been made by relatives of eight cases. They are most frequent shortly after operation and diminish or disappear in the course of time. They have been neither of an intensity nor incidence to justify serious consideration. . . Schizophrenic defect states of standard pattern, however, are seen in about the proportion that would be expected from a series of nonlobotomized schizophrenic patients." Worthing speaks from an experience of close to a thousand patients. Re-

cently, about half of the patients subjected to operation have been able to return to the community.

Abely¹ in the same symposium with Baruk believes that psychosurgery should not be placed in a special category, "nor should obstacles be multiplied that might oppose its action so remarkably beneficent in so many cases."

Psychosurgery has been banned in the Soviet Union by decree of the Ministry of Health.³² This decree states that use of prefrontal lobotomy for the treatment of psychiatric disorders contradicts fundamental concepts of Pavlovian theory; that lobotomy has no greater value than other methods but leads to irreversible organic changes precluding further treatment of the disease.

Meanwhile, the number of lobotomies and kindred operations in this country is approaching the twenty thousand mark. Fulton²¹ states: "The possibility inherent in lobotomy for returning the mentally ill to a happier and more useful existence provides one of the most challenging problems in medicine today."

CLINICAL STUDIES

During the past year two important control studies have been reported. The Connecticut group²⁰ examined 254 lobotomized patients at the end of two years and found that 60 per cent showed significant improvement, more than half of these being at home. For controls, they used 100 patients who had been selected for lobotomy on the basis of their psychiatric condition, but whose relatives had refused permission for operation. Of these patients, 95 per cent were unimproved, worse or dead, and only one remained out of the hospital. "Improvement, either by spontaneous means or by the use of shock therapies, is rare after this point [2 years], and it would seem fruitless to delay psychosurgery in appropriate cases much beyond this time. Comparative results in our two groups lead to the inevitable conclusion that lobotomy exerts a beneficial effect that is not achieved by other means in cases of chronic mental illness."

The California group⁴⁹ compared 15 patients subjected to bilateral lobotomy with 16 patients subjected to unilateral lobotomy. Beneficial results were reported in 69 per cent of the bilateral group as against 18 per cent in the unilateral group. Fourteen of the 16 unilateral cases were then reoperated on the opposite side with benefit in 79 per cent. "It is concluded that (a) the psychic trauma of operative intervention is not an important factor in determining the therapeutic benefits derived from a frontal lobotomy, and (b) except in rare instances bilateral operation is necessary for beneficial results in the patient with chronic schizophrenia."

Unpublished observations by the reviewers suggest the possibility that in the "rare instances" in which unilateral operations succeed, the surgeon has penetrated through the genu of the corpus callosum and has produced surgical lesions in the opposite hemisphere.

Transorbital lobotomy is gaining in recognition, and now accounts for approximately one-third of the lobotomies performed.¹¹ Morbidity and mortality statistics are encouraging. Freeman and Williams¹⁹ studied 15 brains at periods up to one year after transorbital lobotomy and concluded that from the pathologic standpoint the operation is a clean-cut, selective procedure for severing the thalamofrontal radiation. Moore²³⁻²⁵ has also employed this procedure in some 300 cases mostly of chronic schizophrenia with improvement in two-thirds of the patients. "It has the great advantage over former methods of lobotomy that it produces no untoward psychological effects. In view of the relative ease of performance, short hospitalization, minimal nursing care, insignificant morbidity, low mortality rate (1.8 per cent), and the favorable results, the author suggests that this procedure be utilized more widely in suitable cases, so that the patients are not unnecessarily relegated to custodial institutions for life or permitted to lead a burdensome existence." Wilson, Pittman and Bennett,⁶⁰ on the basis of 200 exceptionally difficult cases, recommend that transorbital lobotomy "be considered for all chronically disturbed patients in whom other less strenuous forms of therapy have failed after one year." These and other authors report few convulsive seizures, less than one per cent, whereas Drubin¹⁴ who followed 68 patients after open prefrontal lobotomy from one to four years, reported seizures in 32 per cent. Fiamberti¹⁵ calls attention to several conditions in and around the orbit which are contraindications to transorbital lobotomy: (1) Aberrant ethmoid cells with infection. (2) Malformation or thickening of the orbital plate. (3) Osteomas of the orbital plate. (4) Intraorbital tumors.

Among a number of studies covering a large group of case material may be cited one by Tollund⁵⁵ covering 400 patients with the usual one-third recovery.

Those who have employed psychosurgery on chronic hospital cases have established this means of therapy as valid and useful. When it comes to psychoneurotic and psychosomatic illnesses, the problem is still in a state of flux. Sargent⁴⁷ has reported highly satisfactory results following lobotomy in emotionally distressed patients suffering from hypertension, cardiac irregularities, asthma, dermatitis and rheumatoid arthritis. Freeman¹⁸ reported briefly a series of 65 patients in whom obsessive and anxious traits were disabling, and in whom excellent results were achieved in about 80 per cent. The relief of self-directed anxiety appears to be the specific effect of transorbital lobotomy.

Williams and Freeman⁵⁸ relieved a patient of auditory hallucinations by removing the amygdaloid nucleus on both sides.

Special studies of lobotomy have been reported as follows:

Children.....	Fair to poor ¹⁷
Body shape.....	Better in mesomorphs ²⁵
Tuberculosis.....	Good ²⁸
Alcoholism.....	Nine patients worse, three better ⁵⁴

Psychologic studies on lobotomized patients have shown:

Greater sociability ⁶
Improved intellectual functioning ^{23b}
Reduced creative ability ¹³
No distortion of "Draw-a-person" test following thalamotomy ¹⁶
Less sex fantasy ²⁷
Few dreams ³⁹
Failure in the maze test ⁴¹
Reduced hallucinations ⁴⁴
Absence of mental changes after orbital lobotomy ⁴⁵
"Don't care" attitude ⁵⁷
Predictive value of metonym test ⁶³

ANATOMY AND PATHOLOGY

For a long time little was known about the termination of frontal efferent fibers. Beck⁴ studying the *boutons terminaux* after lobotomy, found that corticopontile fibers end high up in the medial portion of the pons, being derived from the dorsal and lateral convexity of the prefrontal region. "The extreme pole and the entire orbital surface do not contribute." No corticonigral fibers originate anterior to area 6. Frontal projection fibers are liberally distributed in the reticular formation of the midbrain and interbrain. Brickner⁸ published a final report on the famous Mr. A. whose frontal lobes were both removed by Dandy in 1930. The patient was substantially unchanged from the time of operation until 1947 when another meningioma growing in the occipital lobe began to exert pressure. The patient died in 1949 and showed many additional tumorous nodules over the dura. There was a small remnant of the original meningioma of the olfactory groove. The level of amputation of the frontal lobes approximated the coronal suture and sphenoidal ridge. Freeman^{16a} compared the myelinated fibers of the frontal lobe of a seven-month infant with the demyelinated area in a patient after lobotomy, finding the contrasting picture, one the negative of the other.

Four monographs on psychosurgery have appeared since the publication

of the second edition of Freeman and Watts *Psychosurgery* in December, 1950, and several more are in preparation. Yahn, Mattos Pimenta and Sette⁶² brought together their previous studies and added two new chapters in a work that carries English summaries. Public Health Service Publication No. 16,⁵ the proceedings of the first research conference on psychosurgery, deals with criteria for the selection of psychotic patients for psychosurgery. It is remarkable particularly for factual data on the extent of the problems, as indicated in the various appendixes. The discussion in the main body of the monograph covers contrasting viewpoints. Singer⁵⁰ reporting fifty cases, advises following lobotomy with insulin shock therapy. Fulton²¹ sketched the physiologic background for psychosurgery and gave many hints of future applications.

PHYSIOLOGY

A number of physiologic changes have been reported following operations on the frontal lobe. After lobotomy, Ax and Greenblatt² found a regular decrease in pulse rate, face temperature and sweating; also a reduction in the inspiration-expiration ratio. These changes are probably attributable to a decrease in anxiety. In a series of schizophrenics, Buck, Carscallen and Hobbs⁹ reported an improvement in temperature regulation. They also found that there is a trend toward weight gain in patients improved by lobotomy, and a trend toward weight loss in those who were not benefited. These findings indicate that an increase in weight does not necessarily follow the operation of lobotomy but is the result of improved appetite accompanied by amelioration of the patient's symptoms. About a month after frontal topectomy Carpenter¹² found a longer latent period between the injection of insulin and minimal blood sugar levels than in controls; and a shorter interval between the injection of subcutaneous epinephrine and maximum blood sugar levels. He observed no demonstrable effect on gastric secretion, but bilateral ablation of area 11 inhibited the secretion of gastric HCl. Electrocardiograms were performed upon 100 psychiatric patients before and after frontal lobotomy by Oltman and Friedman.³⁷ They found that tachycardia was reduced from 6 per cent to 2 per cent; premature beats increased from 3 per cent to 5 per cent. In the course of performing cortical undercutting in mental patients, Liberson, Scoville and Dunsmore²⁸ reported that profound changes in respiration, state of consciousness and delayed appearance of seizures followed stimulation of the uncus with relatively low voltage of short duration. Meager changes were noted following stimulation of the cingulate, orbital and superior surface areas of the frontal lobes.

PAIN

The primary indication for psychosurgery in treating pain is well stated by Murphy.³⁶ "The family physician, supporting the final illness of a cancer case, is often faced with the problem of obtaining symptomatic treatment when consulting colleagues are unwilling to make further efforts to eradicate underlying pathology. It is in this situation that prefrontal lobotomy is urged as a measure best suited to the over-all management of the case." Williams and Freeman⁵⁹ reported 23 cases of intractable pain treated by transorbital lobotomy. They found the operation immediately effective in all cases, but five patients relapsed to a state of suffering within two weeks and two others within three months. The majority of their patients were terminal cases of carcinoma that lived only a few months. Grantham²³ obtained good results in a series of pain patients by interrupting the pathways in the lower mesial quadrants. In addition to carcinoma, Lyerly²⁹ performed bilateral lobotomy in atypical facial neuralgia, posttraumatic headache and in neuritis which persisted after the removal of a cervical disc. Tönnis⁵⁶ had a good result in one case of unilateral lobotomy and a fair result in another. Bonner, Cobb and Sweet⁷ reported a case of post-herpetic neuralgia treated by left orbital gyrectomy and, two years later, a right orbital gyrectomy was performed with a good clinical result. Most writers are of the opinion that the benefits of psychosurgery are largely due to the relief of anxiety and fear of the future and to the euphoria produced by the procedure. Rao⁴⁴ finds lobotomy more effective in patients with marked psychic pain. Fulton,²¹ on the other hand, believes "the operation of lobotomy removes large numbers of visceral pain projections from the sphere of consciousness and this no doubt is the reason why the patient's attitude toward his pain changes."

SURGICAL ASPECTS

The trend in the past year has been toward selective or more restricted operations. The feeling is that with greater knowledge of cerebral function and better selection of patients, it is possible to relieve mental symptoms and pain, but avoid personality change and epilepsy. Fulton²¹ believes that in light of the information we now possess, the "radical lobotomy as carried out by Freeman and Watts and by Lyerly should be abandoned in favor of a more restricted lesion."

In order to ascertain in some degree the amount of relief and of disability to be expected from lobotomy, Putnam⁴³ introduced 10 per cent procaine base in iodized sesame oil. He used the transorbital route rather than the frontal burr holes. Mandl³⁰ has injected 1 per cent procaine hydrochloride into the frontal lobes through frontal burr holes for both diagnostic

and therapeutic effects. Stender⁵³ injected 10 cc. of the patient's own blood by the transorbital method to produce intracerebral hematoma and sterile inflammation. Such chemical lobotomy may be anticipated to forecast the results of surgical operation. It must be remembered that animal experiments have shown that injection of procaine into the ventricles is hazardous.

In a symposium on the operative treatments of mental disorders, Cairns¹⁰ found that cingulectomy was useful in anxiety states and obsessive tension states but was not effective in psychotic patients. According to Fulton,²¹ Livingston has obtained satisfactory results in about one-third of the psychotic patients with bilateral cingulectomy.

Seeking a more restricted operation, Siris⁵¹ introduces thalamocingulate faciculotomy, having in mind the role of the cingulate gyrus in emotion. It appears to afford significant relief of symptoms without gross impairment of higher faculties. Grantham²³ attacks the inferior mesial quadrant of the frontal lobe by electrocoagulation. He verifies the location of the electrodes by x-ray at the operating table.

For the purpose of comparing the results with his series of 1800 standard operations, McKissock³¹ has performed what he terms rostral leukotomy. In one group operated on by the open method and a second by the blind method, he cuts the white matter in a plane about 2 cm. anterior to the coronal suture. He concludes that rostral leukotomy may be used in states of tension in depressive or obsessional patients and for hypochondriasis, but that the Freeman-Watts technique is still the operation of choice in most cases of mental illness requiring surgical treatment.

In analyzing their results in selective cortical undercutting, Scoville, Wilk and Pepe⁴⁸ find little evidence of specificity of the frontal lobes in their effect on psychoses, but definite specificity in their effect on personality. The personality is little affected by isolation of the orbital surface, but definite blunting occurs upon isolation of the superior surface, but less than that found after standard lobotomy. They recommend undercutting the orbital surface for psychoneurosis and pain. For schizophrenia it may be necessary to undercut the superior surface. Technically, undercutting the cingulate gyrus is more difficult and dangerous.

Further experience has led Pool and LeBeau to the conclusion that a single type of topectomy is not applicable to all cases. Pool⁴⁰ expresses the opinion that the optimum removal for pain is 20 to 25 grams; for affective conditions 30 to 35 grams; for dementia praecox 35 to 40 grams in non-deteriorated individuals and 40 to 50 or more in deteriorated cases. Le Beau²⁶ also describes the areas which should be excised for different mental conditions and points out the surgical uncertainties of prefrontal topectomy and lobotomy.

A new stereoecephalotome (Model III) has been developed by Spiegel,

Wycis and Thur⁵² which has advantages over the previous models: (1) relatively low weight; (2) it can be easily mounted on the skull at operation in exactly the same position as at the preoperative x-ray study; (3) it has multiple electrode holders and electrodes may be inserted into the brain from the top, the dorsal or either lateral aspect of the skull. Hayne and Meyers^{23a} have also built an improved stereotaxic instrument with vertical and horizontal electrodes.

The foregoing modifications of lobotomy have been undertaken in a determined effort to achieve relief of suffering without at the same time producing undesirable personality alterations. In the reviewers' opinion the various restricted operations are ineffective in chronic schizophrenia.

REFERENCES

- ¹ Abely, X.: Le consentement à l'acte psycho-chirurgicale. *Ann. méd.-psychol.* 1:465-472, 1951.
- ² Ax, A. F. and Greenblatt, M.: Physiological changes following frontal lobe surgery for chronic mental illness. *A. M. A. Arch. Neurol. & Psychiat. Tr. Boston Soc. Psychiat. & Neurol.* 66:805-806, 1951.
- ³ Baruk, H.: Les problèmes médico-legaux et moraux posés par la psychochirurgie. *Ann. méd.-psychol.* 1:472-474, 1951.
- ⁴ Beck, E.: The origin, course and termination of the prefronto-pontine tract in the human brain. *Brain* 73:368-391, 1950.
- ⁵ Bigelow, N. ed.: Criteria for the selection of psychotic patients for psychosurgery. *Proc. First Research Conf. on Psychosurg. Pub. Health Serv. Publ.* #16. 1951. pp. 173.
- ⁶ Bockoven, J. S. and Hyde, R. W.: Application of sociometric technique to study of lobotomized patients. *J. Nerv. & Ment. Dis.* 114:95-105, 1951.
- ⁷ Bonner, F. J., Cobb, S., and Sweet, W. H.: Orbital gyrectomy for intractable pain. *Arch. Neurol. & Psychiat.* 66:239-240, 1951.
- ⁸ Brickner, R. M.: The brain of patient "A" after bilateral frontal lobectomy and comments on the status of the frontal lobe problem. *Tr. Am. Neurol. A.* 75:33-37, 1950.
- ⁹ Buck, G. W., Carscallen, H. B., and Hobbs, G. E.: Effect of prefrontal lobotomy on temperature regulation in schizophrenic patients. *Arch. Neurol. & Psychiat.* 65:197-205, 1951.
- ¹⁰ Cairns, H. et al.: A symposium on the operative treatment of mental disorders. *Oxford Med. School Gazette.* 3:3, 1951.
- ¹¹ Cantzlaar, G. L. ed.: Proceedings of the third research conference on psychosurgery. In press.
- ¹² Carpenter, M. B.: The influence of frontal topectomy upon gastric secretion; review of data on 24 cases and 14 controls. *J. Nerv. & Ment. Dis.* 113:52-60, 1951.
- ¹³ Dax, E. C.: Effets thérapeutiques des lobotomies. L'opération de la leucotomie et l'activité créatrice en peinture. *J. brasil. psiquiat.* 1:310-318, 1951.
- ¹⁴ Drubin, L.: Further observations on sixty-two lobotomized psychotic male veterans at the Veterans Hospital, Northport, New York. *J. Nerv. & Ment. Dis.* 113:247-256, 1951.
- ¹⁵ Fiamberti, A. M.: Indagini radiografiche nella leucotomia transorbitaria. *Rass. neuropsic.* 5:1-7, 1951.

- ¹⁶ Freed, H. and Pastor, J. T.: Evaluation of the "Draw-a-person" test (modified) in thalamotomy with particular reference to the body image. *J. Nerv. & Ment. Dis.* 114:106-120, 1951.
- ^{16a} Freeman, W.: Die thalamo-frontalen Verbindungen im Licht der präfrontalen Lobotomie. *Arch. f. Psychiat. u. Ztschr. Neurol.* 185:624-626, 1950.
- ¹⁷ —: La lobotomie chez l'enfant. *Semaine de hôp. Paris.* 27:2403-2405, 1951.
- ¹⁸ —: Lobotomy in the treatment of disabling psychoneurosis. *Picomescio Mail Bag (St. Petersburg, Fla.)* 17:28-33, (Dec.) 1951.
- ¹⁹ — and Williams, J. M.: Lesions of transorbital lobotomy. *Arch. Neurol. & Psychiat.* 66:191-198, 1951.
- ²⁰ Friedman, S., Moore, B. E., Ranger, C. O., and Russman, C.: A progress study of lobotomized and control patients. *Am. J. Psychiat.* 108:10-18, 1951.
- ²¹ Fulton: *Frontal Lobotomy and Affective Behavior*. A neurophysiological analysis. New York, Norton, 1951.
- ²² Glees, P., Cole, J., Whitty, C. W. M., and Cairns, H.: Effects of lesions in the cingular gyrus and adjacent areas in monkeys. *J. Neurol., Neurosurg. & Psychiat.* 13:178-190, 1950.
- ²³ Grantham, E. G.: Prefrontal lobotomy for relief of pain; with a report of a new operative technique. *J. Neurosurg.* 8:405, 1951.
- ^{23a} Hayne, R. and Meyers, R. J.: An improved model of a human stereotaxic instrument. *J. Neurosurg.* 7:463-466, 1950.
- ^{23b} Hoch, P. H.: Personality changes after topectomy. *Psychiatric Quart.* 25:402-408, 1951.
- ²⁴ Kalinowsky, L. B., Freeman, W., et al.: Symposium: A psychiatric evaluation of psychosurgery. *Surg. Gynec. & Obst.* 92:601-617, 1951.
- ²⁵ Kline, N. S. and Tenney, A. M.: Prognosis in topectomies and lobotomies relative to body type. *Arch. Neurol. & Psychiat.* 65:323-325, 1951.
- ²⁶ LeBeau, J.: Surgical uncertainties of prefrontal topectomy and leucotomy (observation on 100 cases). *J. Ment. Sc.* 97:480-504, 1951.
- ²⁷ Levine, J. and Albert, H.: Sexual behavior after lobotomy. *J. Nerv. & Ment. Dis.* 113:332-341, 1951.
- ²⁸ Liberson, W. T., Seoville, W. B., and Dunsmore, R. H.: Stimulation studies of the prefrontal lobe and uncus in man. *EEG. Clin. Neurophysiol.* 3:1, 1951.
- ²⁹ Lyerly, J. G.: Prefrontal lobotomy for the relief of intractable pain. *Am. J. Surg.* 81:526-32, 1951.
- ³⁰ Mandl, F.: Chemical lobotomy for intractable pain. *J. Internat. Coll. Surgeons* 15:276-280, 1951.
- ³¹ McKissock, W.: Rostral leucotomy. *Lancet.* 2:91-94, 1951.
- ³² Ministry of Health, U.S.S.R.: Order prohibiting lobotomy. *Nevropat. psikhiat.* 20:17-18, (Jan.-Feb.) 1951.
- ³³ Moore, M. T.: An appraisal of transorbital leukotomy. *Am. J. M. Sc.* 221:636-643, 1951.
- ³⁴ —, Hill, R. L., and Lutz, W. M.: Transorbital leucotomy in a state hospital program. *J.A.M.A.* 146:324-330, 1951.
- ³⁵ — and Winkelman, N. W.: Some experiences with transorbital leucotomy. *Am. J. Psychiat.* 107:801-807, 1951.
- ³⁶ Murphy, J. P.: Frontal lobe surgery in treatment of intractable pain; a critique. *Yale J. Biol. & Med.* 23:493-500, 1951.
- ³⁷ Oltman, J. E. and Friedman, S.: The electrocardiogram in psychiatric patients

- (including a report of the electrocardiogram following frontal lobotomy). *J. Nerv. & Ment. Dis.* 113:127-135, 1951.
- ³⁸ —: Pulmonary tuberculosis and frontal lobotomy. *Dis. Nerv. System.* 12:284-286, 1951.
- ³⁹ Piehler, R.: Über das Traumerleben Leukotomierter. *Nervenarzt.* 12:517-522, 1950.
- ⁴⁰ Pool, J. L.: Topectomy, 1946-1951—Report on 106 consecutive non-project topectomy operations. *Tr. & Stud., Coll. Physicians, Philadelphia.* 19:49-67, (Aug.) 1951.
- ⁴¹ Porteus, S. D.: Recent research on the Porteus maze test and psychosurgery. *Brit. J. Med. Psychol.* 2:132-140, 1951.
- ⁴² Prick, J. J. G.: Changements de la personnalité consécutifs à la leucotomie. *J. Congr. Mond. psychiat.* 2:4-5, 1950.
- ⁴³ Putnam, T. J.: Procaine base in iodized oil introduced transorbitally as a test for the effects of lobotomy. *Tr. Am. Neurol. A.* 75:125-128, 1950.
- ⁴⁴ Rao, B. N. B.: Prefrontal leucotomy for intractable pain. *Indian J. Surg.* 13:132-137, 1951.
- ^{44a} Reiner, E. R. and Sands, S. L.: Lobotomy and psychopathology. *Arch. Neurol. & Psychiat.* 65:48-53, 1951.
- ⁴⁵ Rylander, G.: Observations on mental changes after total lobotomy and after inferior lobotomy. *Acta psychiat. et neurol. Suppl.* 60:82-89, 1951.
- ⁴⁶ Sargant, W. and Slater, E.: Physical methods of treatment in psychiatry. *Brit. M. J.* 1:1315, 1951.
- ⁴⁷ Sargant, W.: Leucotomy in psychosomatic disorders. *Lancet.* 2:87-90, 1951.
- ⁴⁸ Scoville, W. B., Wilk, E. K., and Pepe, A. J.: Selective cortical undercutting. Results in new method of fractional lobotomy. *Am. J. Psychiat.* 107:730-738, 1951.
- ⁴⁹ Simon, A., Margolis, L. H., Adams, J. E., and Bowman, K. M.: Unilateral and bilateral lobotomy; a controlled evaluation. *Arch. Neurol. & Psychiat.* 66:494-503, 1951.
- ⁵⁰ Singer, L.: La psycho-chirurgie des névroses et des psychoses. Strasbourg, 1951, Imp. d. dernières nourelles.
- ⁵¹ Siris, J. H.: Thalamo-cingulate fasciculotomy. *Psychiat. Quart.* 25:251-6, 1951.
- ⁵² Spiegel, E. A., Wycis, H. T., and Thur, C.: The stereoencephalotome. (Model III of our stereotaxic apparatus for operations on the human brain.) *J. Neurosurg.* 8:452, 1951.
- ⁵³ Stender, A.: Ueber die transorbitale Leukotomie und eine neue Variante (intrafrontale Eigenblutinjektion). *Nervenarzt.* 12:514-517, 1950.
- ⁵⁴ Talbot, B., Bellis, E. C., and Greenblatt, M.: Alcoholism and lobotomy. *Quart. J. Stud. on Alcohol.* 12:386-394, 1951.
- ⁵⁵ Tollund, B.: Results of 400 frontal lobotomies in cases of chronic psychosis. *Nord. med.* 45:181-183, 1951.
- ⁵⁶ Tönnis, W. and Kreissel, H.: Die Bedeutung einer sorgfältigen Differentialdiagnose für die chirurgische Behandlung der Trigeminusneuralgie. *Deutsche med. Wehnschr.* 76:1202-1205, 1951.
- ⁵⁷ Vicor, M.: Personality changes following prefrontal leucotomy as reflected by the Minnesota multiphasic personality inventory and the results of psychometric testing. *J. Ment. Sc.* 97:159-173, 1951.
- ⁵⁸ Williams, J. M. and Freeman, W.: Amygdaloidectomy for the suppression of

auditory hallucinations. A preliminary report of a theory and its application in one case. *Med. Ann. District of Columbia*. 20:192-196, 1951.

- ⁵⁹ —: Transorbital lobotomy in the relief of intractable pain. *Arch. Surg.* 63:203-210, 1951.
- ⁶⁰ Wilson, W. W., Pittman, A. R., and Bennett, R. E.: Transorbital lobotomy in chronically disturbed patients. *Am. J. Psychiat.* 108:444-449, 1951.
- ⁶¹ Worthing, H. J., Brill, H., and Wigderson, H.: Evaluation of immediate and late results of prefrontal lobotomy in 600 cases, including a case of post-encephalitis and other organic states. *Am. J. Psychiat.* 108:328-336, 1951.
- ⁶² Yahn, M., Mattos Pimenta, A., and Sette, A., Jr.: *Tratamento cirurgico das molestias mentais (Leucotomia)*. São Paulo, 1951, Edigraf.
- ⁶³ Zubin, J. and Windle, C.: The prognostic value of the metenym test in a follow-up study of psychosurgery patients and their controls. *J. Clin. Psychol.* 7:221-223, 1951.

IV. PSYCHIATRY

CHAPTER 22

Clinical Psychiatry

By ALEXANDER SIMON, M.D.

IN HIS presidential address, at the 107th annual meeting of the American Psychiatric Association, John C. Whitehorn²²² commented on the period of growth and struggle in the Association. He mentioned in particular the Mental Hospital Institutes, the Mental Hospital Inspection Service, the work of the committees of the Association, and the interest of American psychiatrists in the social implications of psychiatry. "This zeal to project psychiatry onto social problems has sometimes outrun good judgment. It is as if promissory notes had been circulated, in the name of psychiatry, beyond our present ability to make good on them." Eaton,⁴⁸ in a stimulating paper, discusses the question, "What is mental health?" and says, "Unfortunately for both patients and society, social scientists and medical men are equally far from a scientific understanding of mental illness."

He believes mental health, as a scientific concept, does not now exist. Research in this field is faced with obstacles of theory that limit the potentiality for clarification, and he emphasizes that mental health is part of general health, and that a study of mental health must take place within the total pattern that ties culture and personality into a functioning entity. Environmental frustrations in which some persons respond in some ways that are "not healthy" are the same occasions through which others demonstrate what is considered "normality." Mental health is, therefore, not the absence of frustration. Rather, it shows itself in the manner of handling frustration, and because mental health is a matter of degree, this imposes inexactness. Eaton believes that it is an unwarranted assumption that knowledge derived from acute mental diseases can provide good clues to the causal factors of positive mental health; and finally, that health is not a static quality, since it changes through time. Several criteria of mental health are mentioned by him: mental health as judged by clinical insight; mental health as an ideal type personality description in terms of social

function and maturity; mental health as a self-judgment; mental health as a group judgment; and mental health as a statistical norm. Mental health is a conceptual abstraction, the predominant value judgment in each situation determining which criterion is given the greatest weight.

It is emphasized by Bartemeier¹² that our accomplishments in the field of international understanding have more to do with our interest and our widening sense of responsibility toward these larger human problems and less with any new psychologic discoveries or additions to scientific knowledge. The first contribution of psychiatry to international understanding has been the establishment of lines of communication between psychiatrists working in many different countries; the second with the interdisciplinary or multiprofessional method of studying various universal problems in the field of mental health. "It must be clear that the psychiatrist is not a practical sociologist and is not a magician who by virtue of his knowledge of the psychology of men could be considered as holding the key to world understanding." Several papers have been written concerning such general concepts as national characteristics and international relations; the scientific study of bipolar attitudes; the contribution of history to international understanding; the relationship between culture and personality; and the methods of the social sciences in the approach to international problems. Klineberg¹¹⁰ notes that the various studies on national characteristics fall into several types: those directed toward establishing the general pattern of the national culture and its effect on personality; an approach that is concerned with the examination of a number of individuals within a particular nation and which notes the differences as well as the similarities between such individuals; and an intermediate approach that utilizes some of both of the first two. The author comments on various methods by which one makes judgments about the psychologic characteristics of culture, mentioning the questionnaire method, the Rorschach technic and intensive interviewing, modified from the psychiatric and psychoanalytic interviews in clinical use. The principal features of the current world situation are discussed by Lasswell,¹¹⁸ who emphasizes that the psychologic structure of totalitarian systems makes for war, and that the expectation of "inevitable" war does not make war in fact inevitable, and that the bipolarity of international politics does not make war "inevitable." The point of view of the historian is developed by Ehrmann⁴⁶ who believes that within limits, men in positions of responsibility and authority still exercise some measure of choice, and that these determinations may avert as well as bring about a war; and that the work of the psychiatrist on psychopathologic factors making for war—the mass mind, fears, anxieties and sense of insecurity of peoples, and the role of leadership—can find its place in a synthesis of fundamental causes of war as it can in the tracing of the immediate back-

ground of interstate tensions and conflicts. Brown²³ states that when we talk about culture, society and personality, we are talking about different aspects of the same phenomena. Society is not an abstraction that can ignore individuals, but is a collectivity composed of individuals interacting in an ordered manner, and that each family or each system of interpersonal relationships within a given society is not unique but is a variation of a common pattern. Cultures, or rather society, only change as personalities change, and when we say that "cultures meet" we really mean that people meet. This is further emphasized by Borberg²⁴ who writes, "Unfortunately the anthropomorphizing or the personalizing of the basic concepts of state, nation, country, people (which are results not of a biologic, but of a historical development), blurs the whole picture of things as they are. Full understanding of the fact that these concepts are not realities, but that the individuals who handle these concepts on our behalf are the realities, will in what is called 'international life' increase the responsibility where it ought to be increased, in the life of the significant individuals, the policy-making leaders." There is much similarity between the processes of the psychiatrist-patient relationship in psychotherapy and the scientist-informant relationship in social research. The personal interactions, values, moral standards, and motivation of the social science research workers, as well as their subjects, have a definite bearing on research results and their interpretation. (Eaton and Weill⁴⁴)

Binger¹⁵ asks questions concerning public education in psychiatry. "Is it possible? Is it desirable?" He contends that people should be given insight into normal behavior and relationships, into conditions in State hospitals and the need for clinics and outpatient care, but that as little anxiety and guilt should be raised as possible. Public education is a step in the prevention of mental illness. What the public thinks of psychiatry is discussed by a journalist, Miss June Bingham,¹⁶ who offers her feelings about what a psychiatrist is like and her reaction to the psychiatrists whom she met at a meeting of the American Psychiatric Association.

Several papers have appeared on the subject of the relationships between religion and mental health. The Reverend James Vanderveldt²¹⁷ remarks on the fact that language is a peculiar stumbling block in a meeting between psychiatrists and representatives of religious denominations. While all may speak English, semantic difficulties occasionally handicap mutual understanding because there is a confusion between the roles of ethics and religion. He considers that it is useless to speak of religion in general, as it has two entirely different connotations, the theistic and non-theistic religion. He remarks that one of Freud's objections to religion was that it teaches dependency on God, which indeed it does, and Freud felt that this dependency on God was not good. However, a number of psychiatrists have begun to

realize that independency and self-sufficiency may be just as unhealthy and neurotic as some forms of dependency. In that psychiatry offers methods and technics for the treatment of the mentally ill, religion can be no substitute for psychiatry, although since religion primarily aims at bringing people closer to God, by doing so it may secondarily promote mental health. It is Boisen's²¹ belief that the development and validation of religious faith is a vital part of the social process, and that religious belief is fundamental to the ways of living and working together which characterizes any particular social heritage. He develops the theme of how a new belief comes to be gradually accepted by an increasing number of believers. He remarks about the surprising feature of the failure of the humanistic sciences to carry their inquiries to the level of the religious, and the failures of the students of religion to make use of the methods of science in the study of religious beliefs and the experiences in which they are rooted.

In a historical note,⁹¹ it is observed that the term psychiatry first appeared in Heinroth's *Lehrbuch der Störungen des Seelenlebens*, published in Leipzig in 1818, where there is a passage with the word "Psychiatrie" in it. In another historical note,⁹² Dr. Edward L. Margetts has called attention to the word psychiatry appearing in the first volume of *Beiträge zur Beförderung einer Kurmethode auf psychischen, Wege*, published 10 years before Heinroth's book. Galdston,⁶⁵ in an exposition of the place of Freud in modern day psychiatry, discusses Janet, Pavlov and Adolf Meyer. A comment³⁶ in the *American Journal of Psychiatry* on "Gobbledygook in Psychiatric Writing," states that "new words and concise delineations cannot be avoided and are often indispensable. But involved, long-winded, redundant, tautological, 'obfuscating' language, to which the name gobbledygook has been applied, can, and should, be avoided."

A revised edition of *Principles of Abnormal Psychology*, by Maslow and Mittelman¹³² has been published during the year. This is an excellent survey on psychologic disturbances, the new edition containing new sections on the nature and form of psychologic disturbances in children and old age, on character disturbances, reactions to conditions of war, and somatic methods of treating mental disorders.

During the year, a revised edition of *Nature and Treatment of Mental Disorders*, by Moore^{143a} was published. It includes a section on "The Nature and Treatment of Homosexuality."

The 7th edition of *Practical Clinical Psychiatry*, by Strecker, et al.²⁰⁵ is now available. Included in this is a new chapter on "'Support' Psychotherapy," particularly aimed at the general practitioner, to assist him in handling psychoneurotic and psychosomatic patients that he may see in his office.

Ruesch and Bateson¹⁷¹ present a thought-provoking volume entitled,

Communication, the Social Matrix of Psychiatry, in which the general theme of values, communication, and culture are discussed.

*The Collected Papers of Adolf Meyer*¹⁴⁰⁻¹⁴² in three volumes, include his papers on neurology, medical teaching and psychiatry, and should be a part of every psychiatrist's library.

SCHIZOPHRENIC REACTIONS

Clinical Studies. There is no doubt that the concept of schizophrenia is gradually widening in scope in psychiatric circles in the United States. Langfeldt,¹¹⁷ Professor in Medicine at the University of Oslo, Norway, however, remarks how the diagnostic concept of schizophrenia varied from one clinic to another in the United States. He strongly emphasized the necessity of separating as a special group those cases in which, as shown by catamnestic studies, the disease runs a course different from that in cases characterized by the Kraepelinian symptomatology. He made a followup study (6 to 10 years after discharge) of 100 cases of "typical" schizophrenia as compared with a similar number of cases of "doubtful" schizophrenia. Of the 100 cases of "typical" schizophrenia, 66 were found to be unimproved or worse; 13 improved; 4 cured with defects; and 17 completely cured. A study of these 17 cases, however, revealed that on the basis of the development of initial symptoms of the disease, 14 of them should have been diagnosed as "doubtful" schizophrenia "calling for one or two question marks after the diagnosis." Among the 100 cases diagnosed as "doubtful" schizophrenia, 43 were unimproved or worse; 25 were improved; and 32 completely cured. Among the cured cases there was only one in which the disease might be considered a psychosis of the same nature as those in the previous group which resulted in "defective" states; while among the 43 unimproved cases there were not less than 36 cases that according to the development and symptomatology of the disease should have been diagnosed as "typical" schizophrenias. The author emphasized that a diagnostic differential may be very difficult during the initial stage of the disease. By "typical" schizophrenia he apparently means the Kraepelinian type of dementia praecox. He believes that the term "schizophreniform" should be used for the "doubtful" cases of schizophrenia, and he mentions that he has already given conclusive proof that fundamental variations in blood picture, basal metabolism, adrenalin-pilocarpin and atropine reactions, etc., exist between the various Kraepelinian dementia praecox groups, and that varied somatic pictures may be encountered depending upon the phase of the disease in which the examination is made!

In the discussion of the problem of diagnosis in paranoic disorder, Bonner²³ emphasizes that there is a current tendency to diagnose paranoia as paranoid schizophrenia, and to place the two in the same diagnostic

category. Paranoia, he believes, is far more common in the general population than many investigators realize. He refers to the two forms of the paranoid (or paranoic) syndrome as true paranoia and paranoid condition, and reserves the term paranoid to paranoid schizophrenia. Paranoia is "characterized by persistent systematized delusions, the preservation of the personality, absence of hallucinations, and heightened affectivity, particularly hatred." Paranoia or paranoid condition lacks the extreme logical systems of paranoia, but it seldom exhibits the fragmentation and bizarre delusional trend of paranoid schizophrenia. To render differential diagnosis of these two psychoses more accurate, he considers sociogenic, psychogenic, and associative trends to be important factors. The paranoic patient has grown up in an atmosphere of suppression, harshness, hostility, and brutality, while the paranoid schizophrenic is less likely to have been reared in this type of home. The past history of the paranoic patient is replete with such crises as failure, divorce, and the loss of a loved one, and because of boundless ambition, he drives himself to achieve goals that are beyond his capacity. The paranoid schizophrenic, on the other hand, lacks the intense drive for achievement of the paranoic individual and has fewer failures. The paranoic patient is plagued by domestic conflict, while the paranoid schizophrenic's married life is not as full of marital discord. Often, he does not marry. Paranoics are, for the most part, predominantly extraverted, while paranoid schizophrenics are introverted. Paranoic patients are generally dominant, and show frequent examples of anger and rage, while the paranoid schizophrenics are submissive and display indifference. The paranoic patients generally rate much higher than paranoid schizophrenics on standard intelligence tests. The author's data also indicated the presence of repressed homosexual compulsion in paranoid patients, and more overt homosexuality in paranoid schizophrenics who frequently experience "homosexual panic" which is usually absent in the paranoic.

Psychotic reactions due mainly to unusual external circumstances, such as those occurring in prison or to stress, are often of a paranoic character. A number of young men of Polish nationality were studied by Kino.¹⁰⁵ They were all exposed to the extraordinary physical and mental stresses of war and captivity, but when transferred to England all the danger and strain of war and captivity were removed. As long as they continued to live within their own unit, they felt well and relatively contented, but when transferred to workshops where they found themselves isolated in a foreign environment, every attempt at interpersonal approach was difficult. Misunderstandings and miscomprehensions evoked their suspicion and distrust, and this morbid state of mind grew to such intensity that a rational appreciation of the environment became impossible. The sudden loss of habitual companionship, the foreign surroundings with incomprehensible

atmosphere and habits, the change of occupation, the hazards of being on their own, were too great emotional stresses for them, which finding no relief by verbal expression or sympathetic consolation, broke through as a paranoid psychotic reaction. Seitz¹⁸⁶ differentiates paranoid schizophrenic patients in terms of their reactions to accusation, including their own projected judgments of guilt. He believes that one group actively and defiantly resisted such accusations and projections, and the other passively accepted them, and that this dynamic factor was of prognostic significance. The defiant type was three times as common as the compliant; the prognosis for the compliant type was significantly better than for the defiant; electroshock treatment did not significantly improve the prognosis in the defiant type, but there was a suggestive trend toward improvement in the compliant type. In the defiant type of paranoid schizophrenia, 80 per cent of the patients will not achieve early remission, but in the compliant type, 50 per cent achieve early remission regardless of the type of treatment employed, and as many as 75 per cent will recover if electroshock therapy is used. In a very well presented paper, Noble¹⁴⁹ describes the hysterical manifestations in schizophrenic illness. This syndrome has been called situational psychosis, hystericopsychosis, and pseudoschizophrenia. The study included six patients, three of whom were treated intensively with psychoanalytic psychotherapy. The hysterical symptoms included conversion symptoms, fugue, and twilight or somnambulistic states, marked exaggeration of physical symptoms, with dramatized behavior, autistic preoccupation, and transient delusional and hallucinatory experiences. Their illnesses had been apparent to the patients for most of their lives, during which periodic recurrences of depression, preoccupation, and conversion symptoms occurred. Previous episodes of illness had been met with such maneuvers as changing schools, spending long periods in bed, or returning to live at the home of a patient's mother. Concern about physical health was usual and psychosomatic symptoms common. An appearance of calm and self-absorption had often varied with outbreaks of screaming and disturbed behavior in response to direct frustration. The patient's central problems were associated with unresolved anxieties in relationships with their mothers. The mothers themselves frequently manifested conversion symptoms and demanded attention by hysterical outbursts. Most of the patients encountered marked difficulties in dealing with their own children, toward whom they continued to behave as their mothers had behaved toward them. The father was an inadequate person, the secondary figure in the family, and much depreciated by the mother. Recognition of affection for and erotic interest in the father appeared late in the analysis, but it then became clear that a powerful attachment to the father had seriously vitiated the patients' relationships with men. These patients did not ex-

perience frank psychoses, although periods of disturbances were manifested which closely resembled schizophrenia. The author concludes that there exists a continuum of disturbances ranging from the frank hysterical illness to the disorganizing schizophrenic process, and including the hysterico-psychoses. In another paper, Noble¹⁵⁰ reports on his study of the dreams of schizophrenic patients, and states that there are no dreams characteristic of schizophrenia. The character of the dreams was less dependent upon the nature of the illness than upon the personality and maturity of the patient and the state of the relationship with the therapist. He feels strongly that the interpretation of symbols and the use of free association around symbols is of no value in the treatment of schizophrenia.

The differential diagnosis between a psychotic reaction and psychotic reaction with mental deficiency is important because of implications regarding prognosis, treatment and compensation benefits. In a study of 21 patients, Drubin and Singer⁴¹ observed that re-examination of those patients who had been given a diagnosis of psychosis with mental deficiency revealed that mental deficiency could be excluded in 17 of the cases. Schmideberg¹⁸¹ mentions that Freud himself expressed scepticism about the value of psychoanalytic therapy in the psychoses, stating that psychoses seem to have a nucleus similar to that of cancer that resisted therapeutic efforts. The author describes a case of agoraphobia which was a disguise for a schizophrenic psychosis. After one year's treatment, the agoraphobia was eliminated, but a benign addiction took its place. St. Clair¹⁷⁷ notes that psychotherapy is not different with Negro patients than it is with white. He remarks that the frequency of functional illnesses, the attitudes of suspiciousness and submissiveness, the constancy of race-consciousness, the difficulty in achieving expression of hostility toward the therapist, the tendency to "act out," the emphasis on somatic complaints, and the recognition of social, economic and cultural levels are important in understanding the Negro patient.

Münchausen's syndrome is described by Asher⁹ in a group of cases who are hysterics, schizophrenics, and psychopaths, and who "like the famous Baron von Münchausen, the persons affected have travelled widely, and their stories are both dramatic and untruthful." A form of induced psychosis is described by Tolsma.²¹¹ Darr and Worden³⁸ state that the syndrome of early infantile autistic disorder has been well delineated, but that little is known about the subsequent adjustment of autistic children. They describe a patient who displayed the symptoms of infantile autistic disorder as a child and whose development was observed for a 28-year period, and who is still quite overtly schizophrenic. The relationship between religion and psychiatric disorders is discussed in the cases of four nuns who were patients in a State hospital (Pearson and Ferguson.¹⁵⁵) In considering the

reasons why these women became nuns, the authors submit that each one was looking for the satisfaction of deep inner longings, but since their inner needs were so great, and the convent was unable to fulfill them, the women had recourse to fantasy, and ultimately to psychosis. In the psychoses of nuns, it is not the nun as a nun, not religion except as a stress, but the intrinsic defect within the personality structure of the person that is important. Sechehaye¹⁸⁴ describes a new method of psychotherapy applied to a case of schizophrenia, which she calls "symbolic realization," and in another book¹⁸⁵ she gives the autobiography of a schizophrenic girl as interpreted by her in analytic treatment.

In his *Primer for Psychotherapists*, Colby³⁵ has a chapter on the treatment of schizophrenias. Although his book is an excellent elementary manual for the beginner in psychotherapy, the section on schizophrenia is not up to the high level of the rest of the volume.

Psychopathology. There is no doubt as to the confusion about the concept of the terms "psychosis," "psychoneurosis," and "neurosis" according to Bowman and Rose.²⁵ The terms have been distinguished on the basis of different etiologies, clinical pictures, and prognosis; of quantitative differences in symptomatology; and of qualitative differences in symptomatology. Sometimes they are distinguished by such terms as "major reactions" and "minor reactions," or refer to legal and social differences or committability or lack of committability. Finally "psychosis" is often used synonymously with the term "schizophrenia." Janet was one of the first to emphasize that the terms "psychosis" and "neurosis" referred to an administrative rather than a scientific distinction, emphasizing that any difference between the two terms was purely theoretic. In an excellent survey of comparative psychiatry, Yap²²⁸ states that the detailed symptomatology of such broad syndromes as the schizophrenic, affective and organic reactions are seen in all cultures, but the detailed symptomatology may vary according to prevailing beliefs, customs, interests and conflicts. He describes certain diseases distinguishable from the major types which are peculiar to particular cultures, but which, if they appeared in other cultural groups, would be called abnormal. He gives examples of various kinds of illnesses, such as Koro, found in the Chinese; Lathah, in Malaya; Amok; and the Wihtigo psychosis, among certain Indian tribes of North America.

In discussing the precipitating factors in neuroses and psychoses, Gordon⁷⁶ concludes that mental disorders do occur in consequence of disturbing factors of a special nature, which are capable of influencing the feeling-tone of persons whose mentality is potentially unstable by reasons of hereditary or individual morbid predisposition. The number of cases which he presents, however, is so small that it would be difficult to validate his conclusions. In a study of the importance of biographic factors and psychiatric symp-

toms, Wittenborn and Lesser²²⁵ conclude that psychotic manifestations may be part of a process of behavioral disturbance which has a long history and early symptoms, and that if the significance of early behavior could be ascertained, the subsequent development of the individual might be guided and controlled. For example, patients with a history of alcoholism are likely to show symptoms of marked depression, while alcoholism as a symptom of onset is found usually in paranoid schizophrenia. Feelings of persecution tend to be an early characteristic of those developing phobic compulsive symptoms; however, at the onset they are particularly conspicuous among those who present a paranoid condition. Rud¹⁷⁰ emphasizes that schizophrenics have a primary, incomprehensible, social defect, a displaced, reduced self-confidence, and that this is the primary active factor in the process of desocialization in them. The problems of the self in the light of the psychopathology of schizophrenia are described by McKinney,¹³⁴ who believes that the schizophrenic syndrome provides an unusual opportunity for investigating the relation between subject-object relationships and levels of the experiential field, since their exaggerated forms throw them into bolder relief.

Wexler²²¹ states: "In the present state of our uncertainty it seems to be potentially more useful to stick with clinical descriptions involving concrete behavior than to assign attitudinal shibboleths as therapeutic guides. The ways in which such data are then interpreted depend rather largely on the thought model one employs." He concludes that the classical psychoanalytic method for the treatment of a transference neurosis is inapplicable to the treatment of schizophrenic patients. In schizophrenia we are not so much separated from instincts which need to be seduced into less derivative expression, but rather we are separated from a reasonable ego. It is our major task to resurrect this structure. A primitive, archaic and devastatingly punitive superego plays an important role along with strong demands in producing schizophrenic disorganization. Hyroop⁹⁶ suggests that feelings of omnipotence as well as identification and projection are important factors in the understanding of the paranoid reaction. He believes that the goal of psychotherapy is to attempt to encourage in the patient an identification with the therapist and to weaken the tie to the apparently omnipotent figure. A critical survey of various theories concerning the structure of paranoid ideas is presented by Waelder.²¹⁹ In discussing the concept of depersonalization, Krapf¹¹⁶ describes two types of alteration of the self, one which has to do with the self as an object, and the other in which the self is the subject, this latter type presenting "derealization," derealization expressing an attempt to banish from the self an unpleasant affect.

Basing their work on the theories that schizophrenics manifest considerable difficulty in formulating a group of objects into a concept, and that

they manifest great difficulty in shifting from one concept to a totally different concept—in a situation where two different interpretations can be made of the same stimulus objects—Feldman and Drasgow⁵⁸ have developed a visual-verbal test for distinguishing schizophrenics from a general population. Hall⁸¹ has assembled a set of seven tests with both verbal and non-verbal material, in order to assess one of the various aspects of the ability to abstract, follow a rule or principle, classify or think categorically. He concludes that there seems to be a general simplifying tendency in the mental approach in the schizophrenic patient so that the effort required for them to perform conceptual tasks is beyond them. Albee² attempts to ascertain whether there is a relationship between types of delusions exhibited by schizophrenics admitted to a mental hospital and the outcome of treatment. Two types of delusions, persecutory and self-condemnatory, proved to be significant in predicting outcome of therapy. The appearance of self-condemnatory delusions was a favorable sign. Persecutory delusions indicated a poor prognosis because they implied a breakdown or absence of object relationships, while the patient with self-condemnatory delusions is still able to differentiate between himself and the rest of the world no matter how incorrectly. The various symptoms peculiar to schizophrenia, including the schizophrenic disintegration, may be partly explained on the basis of the weakness of the ego's dynamic energy in certain predisposed individuals, according to Lingjaerde.¹²⁵ Garcia⁶⁶ finds inadequate the various theories which ascribe hallucinations to errors of perception on the basis of thalamic or cortical excitation. Close study of illusions and hallucinations suggest that these have more the character of ideational construction than of perception. He regards hallucinations and illusions as variants of the same fundamental process, "catathymic elaboration," at the expense of affective logic.

Somatic Studies. In his discussion of biochemical considerations of psychotic behavior, Hoagland⁹⁸ states: "It is an article of faith of most students of biology than all human conduct, from the simplest reflex to the achievements of a Newton or a Shakespeare, depends upon the molecular dynamics of the nervous system." He believes that the multiplicity of causes of psychopathologic disturbances can be profitably expressed by the interplay of four main categories of events: genogenic or hereditary causes; histogenic causes or those related to visible lesion of the tissue; chemogenic causes due to molecular changes in tissue function and structure; and psychogenic causes due to maladjustments in interpersonal relations. Present histologic procedures cannot reflect the subtleties of chemical dynamics in the living tissues, and these negative results have very little bearing on the possible role of genetic and chemical factors that may be involved in the psychoses. He reinvestigates the importance of enzyme energetics, brain respiration,

the effect of barbiturates, cyanide and carbon dioxide on brain respiration. He remarks that the part of the brain where one may most likely find molecular derangement of function is probably the hypothalamus.

Himwich⁸⁹ reviews the relationship between brain metabolism in certain abnormal conditions and thought processes and concludes that any defect in the biochemical processes of the brain may make itself known by alterations in cerebral function, including personality changes which may be neurotic or psychotic in character. The oxidation of glucose may be disturbed, the storage of energy in the phosphate bonds may be faulty, and these may be factors in the development of neurotic and psychotic symptoms. He believes that the production of psychotic reactions with ACTH and cortisone should be studied further and that cortisone may affect cerebral enzymatic processes directly. He admits that the so-called "functional" psychoses have resisted all efforts to disclose convincing organic clues, but with the observation that minute amounts of psychochemical agents may evoke a temporary psychosis, it seems possible to determine whether or not these psychoses are also results of a faulty biochemistry.

The thyroid activity of mentally ill patients was studied by Reiss, et al.¹⁶⁴ in a series of 541 patients by means of the radioactive tracer method. Abnormal thyroid values were not characteristic of any single psychiatric disorder, but there are indications of thyroid disturbances in schizophrenics.

In a series of papers, von Ophuijsen, et al.^{174-176, 192, 213, 218} describe the relationship of endocrinology to psychiatric disorders. The present status of histamine biochemotherapy in psychiatry, the importance of sex steroid biochemotherapy in psychiatry, the general biologic findings which point significantly to the metabolic aspects of schizophrenia, and somatic perspectives in psychiatric research are presented.

In order to study the central homeostatic mechanism in schizophrenia, Hill et al.⁸⁶ submitted a series of patients to a homeostatic stress, the adjustment to which would involve the excitability of the sympathetic-adrenalin system, and which would also constitute a significant threat to the functions of the cerebral cortex. For this purpose, insulin hypoglycemia was chosen. It was concluded that the adjustment mechanisms are defective among schizophrenics, but the differences are all a matter of degree and consist of a delayed or inefficient response in schizophrenic patients.

Bullock et al.²⁹ believe that it is possible to make a differentiation between what they call "symptomatic schizophrenia" and "idiopathic schizophrenia." Idiopathic schizophrenia is defined as a disturbance of conceptual thinking, together with a disturbance of affect and hallucinations, and absence or diminution of empathy. The level of blood cholesterol and the level of globulin in the cerebral spinal fluid were considered by these authors to be significantly changed in the so-called "idiopathic schizophrenia."

After a study of 50 psychotic Oriental patients, Morris¹⁴⁵ concludes that there is a relationship between constitutional variations and fundamental psychotic behavior reactions, which hold for psychotics in India and China similar to the results found in patients in the United States. From a study of glucose tolerance in chronic schizophrenia states, Simon and Garvey¹⁹⁵ believe that the schizophrenics display abnormal diabetic-like responses as measured by the Exton-Rose glucose tolerance test. Altschule et al.⁶ report that the rise in blood sugar after the injection of epinephrine was larger than would be expected in patients suffering from schizophrenia, manic-depressive psychoses and severe neuroses. The finding suggests an increased tendency to form hepatic glycogen in these patients in spite of starvation and malnutrition. An intrinsic endocrine defect or vulnerable endocrine system is believed by Friedlander⁶² to be present in schizophrenia. A study by Gottfried and Minsky⁷⁸ of the excretion of urinary total neutral 17-ketosteroid in schizophrenic patients indicates that the mean value for patients upon admission agrees closely with that of normals, although the range for the patients was wider than that for normals. There was an indication, too, that a surge in pituitary-adrenocortical activity may be associated with improvement in the condition of the schizophrenic patient. Stein et al.²⁰⁰ found no statistically significant differences in the physiologic responses of chronically ill schizophrenics to heat stress and ACTH as compared with normal controls and non-schizophrenic patients. Similar results were obtained by Glaser and Hoch⁶⁸ who administered corticotrophin in large doses to six patients and found that the changes in them were essentially no different than those observed in normal controls.

Ritchie¹⁶⁷ concludes that neither adrenergic or cholinergic substances are present in the peripheral venous blood of psychiatric patients in sufficient amounts to be demonstrable with an isolated strip of rabbit intestine. A statistically significant difference between the spinal fluid iron of the acute and that of the deteriorated schizophrenic was found by Lehmann and Kral,¹¹⁹ who assumed that a low iron content of the spinal fluid was indicative of increased brain metabolism and high iron values of the spinal fluid may reflect reduced cellular activity of the brain tissue. An electrocardiographic study of 812 psychiatric patients by Oltman and Friedman¹⁵¹ failed to reveal evidence of unusual incidence of abnormalities. On the other hand, Blom¹⁹ found 42 per cent of the electrocardiograms of 193 psychotic patients to be abnormal.

Altschule⁵ observes that inhalation of carbon dioxide may result in temporary disappearance of hallucinations in some patients with schizophrenia. He states that marked diminution in cerebral blood flow may result in re-appearance of hallucinations in some schizophrenic patients in whom hal-

lucinations were present in the past. When cerebral blood flow is decreased in subjects who never had hallucinations the subjects may experience brief, vivid images of events that happened in the distant past. By determining the changes in blood pressure in response to intravenous epinephrine and mecholyl intramuscularly, Funkenstein et al.⁶³ conclude that when the psychologic picture changes, the physiologic picture changes also. Whether the psychologic changes are affected by electric shock, insulin, psychotherapy, spontaneously or through hospital environment, if the patient's psychologic picture does not change, the physiologic picture does not change.

From a study of 578 psychotic patients, Swartz and Semrad²⁰⁷ conclude that psychosomatic and psychotic disorders do not occur in the same person frequently, and that the psychotic individual does not use a psychosomatic disorder as a mechanism of defense. Malmö et al.¹³⁰ after making electromyographic studies of muscular tension in psychiatric patients under stress, state that psychoneurotic and psychotic patients respond to stress with a greater degree of muscular tension than that found in controlled subject.

The thalamic nuclei in 12 cases of dementia praecox, paranoid type, were examined histologically by special methods and the results of such a study reported by Bateman and Papez.¹³ All showed an old chronic disease of nerve cells filled with large groups of inclusion bodies sequestered in the cytoplasm. In 15 cases of psychoses with mental deterioration, there was always a great loss of nerve cells, as high as 90 per cent of the cell population in the association nuclei of the thalamus. In cases with sensory disturbances, especially those with hallucinations and delusions, there was an acute disruption of nerve cells in the sensory nuclei of the thalamus. In another paper by Papez and Bateman,¹⁵³ the changes in nervous tissues which they have observed in patients suffering from mental disease are summarized. How much their observations are the result of artefacts can only be determined when similar studies are carried out by others.

The cytology of rabbit neurons after "malononitrile" administration was studied by Liu,¹²⁷ who concluded that it is unreasonable to expect this chemical agent to increase significantly the nucleotide and protein content of the cytoplasm of neurons of the central nervous system. He believes that Hyden's concept of rapid depletion of these substances in the cytoplasm during intense functional stimulation and the rapid replacement under the influence of "malononitrile" cannot be supported by controlled cytological experiments.

Schefflen¹⁷⁸ states that the distribution of malignant tumors in institutionalized psychotic patients did not differ in type or situation from those of the general population, except for a suggestive, but not significant, increase of carcinomas of the pancreas in schizophrenic patients.

Pomerat¹⁵⁶ describes a study made on more than 8000 cultures of human

brain cells in vitro from tissues obtained from 121 subjects, most of whom suffered from various psychiatric disorders. He has recorded the rhythmic activity of cells cultivated from explants of human brain in tissue culture by means of time-lapse cinematographic technic. Whether these studies will indicate differences between the cells of mentally ill patients and those obtained from "normals" remains to be seen, but the technical procedure itself is an extremely intriguing one and will no doubt extend our knowledge of neurophysiology and neuroanatomy.

Therapy. Psychotherapy is defined by Reid and Finesinger¹⁶³ as the use of psychologic means to mitigate symptoms, to resolve conflicts, and to improve generally the patient's adjustment. In doing psychotherapy, the doctor makes inferences from both the verbal and nonverbal behavior of the patient, and these inferences are used for purposes of interpretation. But it is necessary to establish the validity of these inferences in order to make reliable predictions or to institute rational therapy. They recommend, in order to increase the reliability of inferences in the psychiatric field, that terms must be more accurately defined, the claim that referents for these terms exist must be verified, and that these referents stand in the empirical relations claimed, must be established.

The general treatment of psychoses is outlined by Solomon¹⁹⁷ and Boc-koven et al.²⁰ who emphasize that most acute psychoses have a high recovery potential; that many acute psychotics, if given reasonably considered care, will improve or recover; that not infrequently recovery is retarded if good care is not provided; and that specific therapeutic methods now available will increase the number of acute psychotics who will be able to carry on relatively satisfactorily in society. Good environmental care forms the basis on which all other treatment should stand, and there should be attention to both the physical and psychologic environment. In a study of 228 cases committed to the Boston Psychopathic Hospital in one year, 80 per cent were discharged. Only 10 per cent remained longer than six months and 16 per cent were discharged within 30 days, the average hospitalization for the entire group being only 63 days, and 40 per cent of those who were transferred to hospitals for more prolonged care were discharged. The author considered the following factors of therapeutic importance: general over-all care, including the hospital atmosphere; a therapeutic attitude on the part of all members of the therapeutic team, including psychiatrists, social workers, nurses, attendants, occupational therapists, recreational workers, laboratory technicians, psychologists, students and volunteers; psychotherapy, individual and group in type; somatic therapies; and social therapy.

Menninger¹⁹⁷ outlines the points to be considered and questions to be answered when a decision is to be made on treatment of a patient on either

an outpatient or hospital status. Included is a skeleton plan for a prescribed program of hospital therapy, including the process of admission and treatment by the psychiatric team—medical and surgical therapy, general nursing management, physical medicine rehabilitation therapy, attitude therapy, the contact functions handled by the social workers, and finally what constitutes a post-hospital treatment plan.

In a stimulating and thought-provoking paper, Eisenstein⁴⁷ describes a class of patients who are descriptively neurotic but dynamically psychotic. These patients make up a large proportion of those seeking psychiatric help, particularly in private practice, and he estimates that 30 per cent were of such borderline reaction types. These patients hold jobs or attend school, enjoy musical or artistic interests, socialize, engage in sexual relations, yet suffer from deficient emotional contact and from a seriously impaired sense of reality. Clinically, they complain of varying degrees of boredom, depression or free anxiety and present abortive paranoid features, transient feelings of reference or depersonalization, often with acute exacerbations which are dynamically rooted in serious psychopathology. The major premise of the author is that the ego or integrating apparatus of the borderline patient is severely involved. This affects his reality testing, personal relationships, emotional reactions and integration and manner of handling unconscious conflicts. These patients are crushed in their basic self-esteem, are reactively self-centered and omnipotent in their feelings. They have a predilection for acting rather than speaking; they poorly differentiate fact from fantasy; they are moved by a primitive sense of the magical; they are ambivalent at best, affect-hungry, masochistically deformed, superlatively sensitive to implied slights or rejections, and ever ready to react by shrinking or running away from anticipated reproach, frustration or temptation implied in any close relationship. When they come to treatment, emotional contact with the therapist is as much feared as sought. They are made anxious by aloofness of manner, yet tend to be suspicious of warmth, and the therapist must, therefore, assume the active and benevolent role of a parent rather than the neutral position of an impersonal analyst. The treatment is outlined in three phases: the initial phase of establishing affective contact; the actual psychotherapeutic alliance; and the period of weaning and adjustment. The low tolerance for anxiety makes for "acting out." In therapy, interpretations should be limited, and the therapist should show a minimum of interest in the patient's fantasy and a maximum of interest in his life situation from which the fantasy is a withdrawal. The author calls attention to selective measures required to handle the patient's fantasy, hostility, homosexual material, acting out and suicidal impulses.

In his remarks on the psychoanalysis of schizophrenia, Eissler⁴⁸ believes

it is essential to distinguish two treatment phases. The first, an acute phase, when the patient's ego feels itself at one with the schizophrenic symptomatology; and the second, the phase of relative clinical muteness, when only parts of the ego are affected and symptoms can be concealed, disregarded, repressed or converted to a bland form. The author believes that the two indispensable criteria of successful analysis of a schizophrenic patient are the permanent loss of emotional states in which the ego loses its full feeling of activity, and proof of true insight. The latter is very difficult to achieve because schizophrenic delusions develop only when the ego and superego converge. Once the superego has added its consent, the ego can divorce the quality of reality from delusional memories only under rare and exceptional circumstances. To speak of the "cure of schizophrenia" is meaningless as long as the patient's disease has not been carefully investigated in terms of the genetic, dynamic and structural aspects.

Szalita-Pemow²⁰⁸ recommends the following in the treatment of schizophrenia: the therapist's capacity to respect the patient's sickness and the patient as a person regardless of behavior; the therapist's ability to understand what the patient does; the intuitive capacity or tact of the therapist in bringing to the patient's awareness the amount of truth or reality that he can stand at any particular moment; the therapist's degree of freedom from prestige needs; and finally, his freedom from feelings that the patient's behavior is a reflection on the therapist.

A case report of a schizophrenic patient who had been hospitalized for six years on a "chronic ward," and the influence of an intense transference on such a patient is described by Arnow.⁸ In his discussion of the therapy and treatment of schizophrenia, Aarons¹ also emphasizes that the treatment of the severely disturbed schizophrenic is divided into two periods: the period of treatment of the fulminating psychosis and the period of emotional re-education. A case is presented by Duhl⁴² to show how a markedly regressed schizophrenic patient, who had not responded to various treatment programs, improved when efforts were made to partially satisfy his regressed needs by means of bottle feedings.

A program of group activity, with all the phases coordinated toward strengthening a group spirit among patients and personnel alike, was instituted by Klemes¹⁰⁹ on a ward containing mostly apathetic schizophrenic patients. The results were increased activity and participation of the patients, heightened morale among both patients and personnel, and a distinct change in the atmosphere of the ward from a dismal, depressing place to a cheerful, friendly one.

A well worked-out and formulated study of need-fulfillment on a mental hospital ward is reported by Schwartz et al.¹⁸³ It is evident that the requests made by patients and the responses to these requests given by personnel on

a disturbed mental hospital ward are highly important for the problem of ward management, for the day-to-day living of the patients, and for the clinical course of the patients. The study revealed, however, that the ward was not all as it had been planned. The physicians, nurses, and aides had been working consciously upon the assumption that need-fulfillment was a most important function of the hospital in attaining its therapeutic goal, and it was a generally accepted principle that a patient should get what he asked for unless there was a clear reason why he should not, and that this reason should be given the patient if his request was refused. It was generally accepted that the hospital staff should go out of its way in taking the initiative to discover and meet patients' needs even when these were unexpressed. But the ward definitely fell short of these generally shared goals. It was clear that every group of people who work habitually together build up a body of traditional, relatively uncritical beliefs and interpretations of what goes on in the group which conceal from them their own ignorance. If the psychiatrist does not recognize that withdrawn patients will meet with rebuff in a higher proportion of instances than active patients, he fails to take into account a significant barrier toward the patient's improvement. There is some basis in reality, therefore, for a withdrawn patient's feeling of being discriminated against.

Goldfarb and Park⁷⁴ discuss the dynamic role of group therapy in the total treatment program of psychotic patients, but emphasize that it is important for the therapist to evaluate his goals in therapy, the primary goal being the development of feelings of personal esteem and ego strength in the patients.

As an alternative to hospitalization, foster care for mental patients aids both the institution and the individual, according to Stykos.²⁰⁶ Simon et al.¹⁹⁴ studied the recognition and acceptance of mood in music by psychotic patients by comparing their ability to recognize feelings of sadness and happiness in music to the emotional response of the same music to normals. The results demonstrated considerable similarity in emotional response to this on the part of both groups, but variations within each group occurred to suggest that the knowledge regarding the psychology of music gained from normal subjects could not be absolutely applied to psychotic patients.

Prados¹⁵⁷ recommends that suitable films may be of great benefit in psychiatric therapy. Passivity and receptivity are increased by the experience of viewing a film. Following it, the group may feel aggressive and hostile toward the therapist since unconscious forces are more nearly conscious. The period of the discussion following the showing of a film must be long enough for the group to abreact the emotion stirred up by the film.

The alteration of accessibility of institutional paranoid patients by the use of scopolamine was studied by Goldner and Forrer⁷⁵ who concluded that scopolamine in doses of .25 to 1.0 mgm. is limited in its effectiveness for interview purposes. The effects of d-isomer of desoxyephedrine on 30 psychotic subjects are described by Hope.⁹⁵ Significant changes occurred in motor activity, mimetic expression and speech, responsivity, affect and feeling. Delusions were more readily expressed. No clinical improvement was seen when the immediate effects of the injection had passed. The effects of desoxycortone acetate and ascorbic acid were studied on 28 schizophrenics and a similar number of controls by Rees and King,¹⁶² who report that there were no significant changes either on clinical observation or by the psychiatric rating scale. When tolserol was administered to 26 psychotic patients by Hecker et al.,⁸⁴ the response fell into five types: the release of blocking to recall and revelation of painful experiences; control of rage or manic type of release; relief of overt anxiety with more logical alignment and expression of mental conflict; a combination of the above three responses; or no response at all. The authors conclude that tolserol is not a therapeutic agent per se, but that it may be valuable in acute combat reactions or pronounced anxiety states. The effects of repeated administration of atropine sulfate to mentally ill patients, including psychoneurosis, manic-depressive psychosis, and schizophrenia, were studied by Forrer,⁹⁶ who reports good results especially in those patients with relatively intact ego structure who exhibited tension states.

Murphy¹⁴⁷ discusses the factors which may lead a patient to resist discharge or produce an exacerbation of symptoms when discharge is suggested. He recommends that the following measures be kept in mind: on admission, there should be definition with the patient of the complaint problem, the reasons for hospitalization, what therapy entails and what its possibilities are. Throughout therapy, current reactions and realistic factors must be kept in mind. The total problem should be appraised thoroughly shortly after admission. Social service assistance should be requested at the beginning of hospitalization. Discharge should be planned ahead and not suddenly sprung on an unprepared patient. The psychodrama of relationships and situations anticipated as difficult after discharge may be useful. A discharge group is a useful adjunct. Adequate support of doctors developing guilt and anxiety in relation to their patients is essential. Therapists should be aware of and scrutinize their reactions to patients and the reasons for the production of anxiety and hostility in them by patients.

Malamud et al.¹²⁹ report on the practical application of a rating scale for quantitative recording of clinical changes in the course of mental disease. This rating scale was used to determine the effects of a series of endocrine preparations in the treatment of schizophrenia, including adrenocortico-

trophic hormone (ACTH), adrenal cortical extract (ACE), and desoxycorticosterone (DCA). The results show that no beneficial effects were obtained from the use of any of these drugs in the particular cases treated in the study.

Cohn et al.³⁴ treated six patients who suffered from severe chronic psychoses refractory to all conventional forms of treatment with cortisone. The first patient presented features suggestive of a toxic psychosis during cortisone treatment, but with reduction of dose he had a good remission. The second patient also showed considerable improvement, but the third showed improvement while being given cortisone, but relapsed completely when cortisone was discontinued. The fourth patient displayed toxic symptoms during cortisone treatment with a satisfactory remission when the dosage was reduced. The fifth patient, who had had a lobotomy without improvement, underwent a well sustained remission under cortisone therapy. The sixth patient sustained a complete remission for seven months after the termination of cortisone treatment. The authors suggest that this study indicates the necessity for further studies on the relationship between the chronic elements of schizophrenic illness and certain deficiencies in adrenal function, and of the effect of cortisone on chronic mental illness.

AFFECTIVE REACTIONS

Aside from the somatic therapy of the affective reactions, there is remarkably little that has been published during the past year concerning them. Rado¹⁵⁹ reviews the psychodynamics of depression from the etiologic point of view and states that the depressed patient is sad, tense, low in self-esteem, retarded physically and mentally, preoccupied with his alleged shortcomings and unworthiness, and at the same time, harbors a deep resentment that life does not give him a fair deal. He interprets the depressive spell as a desperate cry for love, precipitated by an actual or imagined loss which the patient feels endangers his security. The patient over-reacts emotionally to his loss, his guilt and distress being part of an expiatory process through which he hopes to recover what he has lost. The dominant motivation of repentance is complicated by the simultaneous presence of a strong resentment that the lost love object has deserted him, and a coercive rage toward this love object. The extreme painfulness of a depression is explained in this theoretic formulation by the patient's attempts to recover the lost love object by two conflicting methods, coercive rage and submissive fear, the depression being agitated or retarded depending on whether rage or fear is dominant. It is not known why depressive spells subside in time, whether treated or not treated, and the physical basis of depressive mechanisms has not been adequately explored. The author emphasizes that in-

vestigation of the physical and genetic aspects of this emotional reaction may be of utmost importance.

In a series of 53 experiments, Pasquarelli¹⁵⁴ concludes that there could be no modification of the affect by direct hypnotic suggestion without changes in the postural set and/or organic sensation. This invariable linkage demonstrates that the "body language" of the musculo-skeletal system is not merely expressive movement, but includes a generative function depending on its preliminary attitudinal phase. In a study of 379 patients suffering from involuntional illnesses, Tait and Burns²⁰⁹ state that controversy over psychologic and somatic causes appears to be waning, and that there is increasing emphasis being placed on the total life situation. A comment is made on Freud's observation that the initial episode of depression follows the loss of a love object and that this may well be applied to this group of patients if it is indicated that the love object also includes the person's own self. In these patients the history of a recent loss of spouse was often noted, but not as frequently as evidence of unusual concern about the decline of the self. The personality of these people who develop involuntional depression is such that they do not seem free to express strong feelings, either hostile or loving.

Merrell¹³⁹ contends that the diagnosis of manic depressive psychosis is being made less commonly than formerly, and concludes that the definition of the psychosis is less inclusive than before. Statistics on discharges and readmissions confirm the cyclical nature of the psychosis, and there is evidence that women are more severely affected than men in that there is an earlier age of onset and of first admissions in the greater proportion of affected women. Data on twins and the high incidence of manic depressive psychosis among relatives of persons with this psychosis, and the difference in frequency of the psychosis in different populations are further evidence for the role of heredity. The best genetic explanation of this data is that of a single autosomal dominant gene with incomplete penetrance. A syndrome characterized by depressive or aggressive moods and a type of thinking dominated by certain ideas and in fluid transition into paranoid thinking is described by Kamm,¹⁰² who noted such reactions in army hospitals, the acute reactions in all these patients tapering off with individually varying oscillations of mood and paranoid thoughts.

In a study of the psychodynamic motivational factors in suicide, Hendin⁸⁵ describes three groups of suicidal patients: those with spite or desire to force love as a dominant motive, as in the reactive depression and character disorder groups; those who display a loss of the love object as in the neurotic group and the passive, dependent elderly group; and those with overt expressions of guilt who were predominantly schizophrenic. The general problem of suicide is reviewed by Farrar⁵¹ who discusses the legal attitude

about suicide and whether or not a suicidal act in itself is a symptom of mental derangement. He summarizes the symptoms which may be pathognomonic of malignant suicidal motivation as (1) an affect state of severe dejection; (2) premeditation which may extend over a considerable period; (3) deliberate planning and choosing of opportunity; (4) concealment of motive; (5) a single fixed purpose that blots out all contrary impulses; (6) disappointment and censure of rescuers if an attempt is frustrated; (7) repeated suicidal acts until the patient either kills himself or recovers. In order to prevent recurrences of manic depressive illnesses, Stevenson and Geoghegan^{202, 203} recommend four methods: the immediate administration of electroshock at the first sign of an impending recurrence; prophylactic electroshock therapy once a month; leucotomy; or the successful solution of the patient's environmental difficulties.

Noack and Trautner¹⁴⁸ describe the lithium treatment of maniacal psychosis, but emphasize that the treatment is not without danger. A series of 24 patients suffering from depression and agitation were treated with desoxyephedrine by Delgado and Carrillo-Broatch.³⁹ The authors felt that this drug, especially in cases of reactive depression, facilitates and reinforces the action of psychotherapy. Thirty cases of depression were treated with dinitrile succinate by Harris⁸² who describes the treatment as safe, easy to administer, and free from toxic effects, but he could find no clear evidence of any therapeutic value.

ORGANIC REACTIONS

From a series of 1821 cases of brain injury occurring during hostilities between Finland and Russia (1939-1944), Hillbom⁸⁷ noted 81 cases of late traumatic psychoses. Included were 16 cases with dementia, 6 of Korsakow's syndrome, 4 manic depressive psychoses, 5 "reactive" psychoses, 6 paranoid psychoses, and 23 schizophrenic-like psychoses. Three of the 23 with schizophrenic-like psychoses undoubtedly had symptoms before the injury. Of the remaining 20, 17 had definitely suffered a temporal lesion. The author concludes that schizophrenic-like psychoses are not uncommon among "late" traumatic psychoses, that the lesion is often in the temporal lobe, and that the auditory and somatic hallucinations observed in these illnesses may be caused by a post-traumatic state of irritation in the temporal lobe.

The "punch drunk" syndrome with a clinical picture of boasting, underestimation of one's opponent, slowness of reactions, intellectual disturbances, memory defects, etc., is reviewed by Raevuori-Nallinmaa¹⁶⁰ together with two case reports.

Simpson¹⁹⁶ reports the case of a 53-year-old woman who developed a psychosis coincident with a severe attack of measles encephalitis at the age of 16. The psychiatric aspects of disseminated sclerosis as determined in a

study of 100 patients is described by Pratt.¹⁵⁸ No specific premorbid personality type could be defined. Emotional stress antedating the onset or relapse was only occasionally considered of significance. Anxiety, hysteria and psychoses were not found to be prominent features. Emotional lability and intellectual impairment were found only in patients with marked neurologic disability. The use of the Thematic Apperception Test did not suggest an undue incidence of suppressed aggression. A patient, originally diagnosed as hysteria, but who suffered from psychomotor epilepsy as a manifestation of subdural hematoma, is reported by Levin.¹²⁴

According to Schlesinger,¹⁸⁰ mental symptoms are a constant feature of gliomas involving the splenium of the corpus callosum and are the inaugural symptoms in 50 per cent of them. The mental changes include disturbances in intellect, affect, behavior and personality and consciousness. The high incidence of psychiatric manifestations in tumors of the corpus callosum is puzzling in view of the fact that surgical section of the entire corpus callosum does not give rise to any deterioration in mental functions. Undoubtedly, the mental symptoms must be due to involvement of neighboring structures. The case of a 54-year-old man with a right frontal lobe meningioma which was surgically removed in two operations is presented by Kahn and Schlesinger⁹⁹ to emphasize that the personality changes which followed were not only due to the localized effects of specific damage but were reactions of the personality as a whole. There was a persistence of psychotic behavior until new environmental conditions were established and the authors raise the question whether "irreversible" loss in some cases may really reflect failure to provide the proper environment in which the patient can recover. That psychiatric symptoms may be one of the early indications of a brain tumor is emphasized by Soniat.¹⁹⁸ There was a similarity in incidence of psychiatric symptoms exhibited by patients with tumors of the frontal and temporal lobes. Some of these symptoms stem from cerebral damage incident to the tumor, but others appear to be exaggerations of the patient's previous personality.

Schwab et al.¹⁸² describe the psychiatric symptoms and syndromes associated with Parkinson's disease as: those unrelated to parkinsonism; reactive mental disturbances; symptoms caused by medication; and paroxysmal psychiatric disorders probably related to Parkinson's disorder. The psychologic symptoms associated with oculogyric crises comprise formes frustes of neuroses and psychoses.

Apter and Halstead⁷ describe a psychiatric syndrome in essential hypertension cases characterized by changes in personality patterns, especially in relation to the expression of hostility, the willingness to yield to dependent needs, reduction in perfectionistic drives, and associated with mild judgmental and memory defects that are not explained by changes

in cardiovascular status alone. They believe that the appearance of this syndrome signifies the onset of organic involvement of the brain.

Space motion hallucinations and phantom impressions are reported as hitherto unrecorded varieties of hallucinations that may occur in migraine (Lippman.¹²⁶) A case of acute intermittent porphyria with a psychotic reaction, schizophrenic in type, greatly improved by electroshock treatment, is reported by Freeman and Kolb.⁶⁰

Levin¹²² reemphasizes the importance of early recognition of delirious reactions which he characterizes as a psychosis characterized (always) by disorientation, and (commonly) by restlessness, dullness, fear, hallucinations and other mental symptoms. Doll⁴⁰ suggests the term "neurophrenia" in place of brain damage for a total behavior picture where central neurologic impairment restricts the optimum expression of native potential and produces behavior disturbances which are remediable under a favorable regimen. A case of encephalopathy associated with acute diffuse platelet thrombosis and associated with mental symptoms is reported by Hauser et al.⁸³ Severe dementia associated with subacute sclerosing leuco-encephalitis is described by Corsellis.³⁷ Spiegel et al.¹⁹⁹ emphasize that it is not possible to refer emotional reactions to a single circumscribed nucleus within the diencephalon or to its connections with the frontal lobes, but that there exists a multiple representation of this function.

The relation of crimes of violence to psychoses associated with pellagra is elaborated by El Kholy,⁴⁹ of Egypt. On the basis of a psychotherapeutically handled case of acromegaly, Bleuler¹⁸ believes there is a relationship between the somatic and psychologic symptoms and that each expresses a similar kind of disharmony. The psychopathology of amnesia, both organic and non-organic, is described by Siegal.¹⁹¹ Psychological disturbances, such as an acute infectious delirium, or a confusional state or a depressive syndrome, may appear during the course of a brucellar meningo-encephalitis (Roger and Poursines¹⁶⁹).

Alexander⁴ emphasizes that the treatment of organic neurologic disorders frequently entails elements of psychotherapy in the control of psychogenic overlay; in promoting adaptive and compensatory mechanisms; and in attempting to prevent psychosomatic reverberations. He believes that the conclusion is unjustified that because psychotherapeutic measures bring about improvement in certain mental conditions and so-called psychosomatic diseases, these are psychogenic. For example, in definitely organic conditions such as post-encephalitic parkinsonism, improvement of function may occur with psychotherapy.

Since nutritional disturbances are both a cause and a result of psychiatric problems, the psychiatrist should evaluate carefully the nutritional status of his patients. Pellegra, acute confusional states, and neurasthenic-like

states may occur in debilitated persons. In such cases, the psychiatrist has a problem of combined therapy—nutritional correction and psychotherapeutic management (Moriarty.¹⁴⁴)

Special testing procedures involving complex visual discriminations are apt to bring out characteristic deficits in patients with cerebral lesions, but these deficits are not specific to frontal lobe lesions, since they may be even more pronounced following penetrations of the posterior lobe substance (Teuber et al.²¹⁰)

An outstanding volume by Himwich,⁹⁰ *Brain Metabolism and Cerebral Disorders*, is now available. Such subjects as brain metabolism during hypoglycemia, cerebral metabolism during growth of lower mammals, the normal cerebral metabolic rate, therapeutics and their application to brain metabolism, the classification and clinical signs, and a theory of narcosis, as related to barbiturates and other depressant drugs, are clearly discussed.

DRUG ADDICTION AND "DRUG PSYCHOSES"

Three types of toxic psychoses, those associated with infectious fevers, the barbiturate intoxications, and a type precipitated by the administration of drugs for the relief of another clinical condition, are described by Palmer.¹⁵² Wikler²²³ discusses the clinical aspects and treatment of chronic barbiturate intoxication, and recommends that once the diagnosis has been established the drug should be withdrawn slowly, perhaps over a period of one month. When the barbiturate abstinence syndrome has developed, replacement of barbiturates, in doses approximating those to which the patient has been accustomed, will usually prevent convulsions or terminate them if they have already occurred. After the manifestations of the barbiturate abstinence syndrome have subsided, the reduction in dosage should be continued over a period of one month. The psychologic effects of chronic barbiturate intoxication have been carefully studied by Kornetsky.¹¹⁴ Five former morphine addicts who volunteered for the experiment were given sufficiently large doses of secobarbital, pentobarbital or amobarbital to induce continuous mild to severe intoxication for periods varying from 92 to 144 days. Psychologic tests were used to measure changes during periods of intoxication and abrupt withdrawal. During the chronic intoxication period there was a quick decline in ability. Oral administration of drugs produced greatest impairment on performance to tasks involving speed, less impairment in tasks involving copying. There were quantitative and qualitative differences in the effects of barbiturates on different subjects, and the same dose of a barbiturate affected the same subject differently on different days. There was a partial loss of ego control manifested by a greater magnitude of pathologic personality projection in the projective technics used. When the administration of barbiturates was discontinued,

the performance quickly reverted to the preaddiction level. Following sodium amytal narcosis, severe withdrawal effects may occur. According to Alexander,³ who treated patients by this method, in the 24 hours following the abrupt discontinuance of the sodium amytal, somnolence wore off and was followed for a period of 24 to 96 hours of insomnia, tremor, generalized convulsions in 10 per cent of the cases; delusions, incoherent speech, vivid visual hallucinations and unusual sensitivity to sounds. The mental content of this delirious reaction is not a specific effect of the barbiturate, but reflects the psychiatric condition of the patient.

Levin¹²³ criticizes a statement made by others that "normal" individuals are not liable to develop toxic symptoms at serum bromide levels between 100 and 200 mg. per 100 cc., and that mental hospital patients are only slightly more susceptible to bromide effects at comparable levels. He points out rightfully that it is a question not only of what the bromide level is, but how long it has been maintained.

Zimmering et al.²³⁰ report on the study of 22 adolescent boys admitted to the Boys' Ward of Bellevue Hospital, New York City, during the months of January and February 1951, for heroin addiction. These boys had certain personality traits in common: a non-aggressive type of social adaptation; a close relationship with their mothers; weak object relationships with others; omnipotent strivings; a tendency to regression and a readiness to assume a more immature and less socially organized form of adaptation.

A study of results in the treatment of 75 patients admitted to a hospital for the treatment of drug addiction is reported by Knight et al.¹¹¹ The primary drug of addiction was morphine in 34, barbiturates in 24, and other drugs such as heroin, dilaudid, codeine, and demerol in 17 cases. Following a period of general psychiatric hospital care and psychotherapeutic interviews, followup studies 1 to 14 years later revealed that 15 have remained abstinent, 12 are managing better, and that 36 per cent in all appear to have been benefited. Group therapy was used by Johnston⁹⁸ in the treatment of narcotic addicts in an intramural setting over a three month period. Calcium gluconate alone or with barbiturates is recommended by Williams²²⁴ in the treatment of addicts. He describes 16 patients, all of whom received relief in a few minutes from symptoms caused by withdrawal of morphine and its derivatives.

Unusual psychologic reactions occurring during the course of "Antabuse" therapy of alcoholics have been reported by several authors. Usdin and Robinson²¹⁶ report a case whose clinical picture was that of a toxic reaction. In a series of 42 patients, Gottesfeld et al.⁷⁷ noted eight who developed psychotic episodes. Five of these were transitory and responded promptly to the withdrawal of "Antabuse" and three were relatively prolonged. On the basis of these cases, the authors concluded that treatment

with "Antabuse" is contraindicated in projective, hostile individuals who feel threatened by help and who have difficulty in forming interpersonal relationships; in patients with a history of psychotic episodes, or who show indications of incipient psychoses; and in patients with borderline schizophrenic adjustments.

Studies with lysergic acid diethylamide (LSD-25) have been carried out to clarify the physiologic and psychic responses attendant on administration of this drug to schizophrenic patients. The drug produced slight increase in blood pressure, pulse rate, salivation, lacrimation, deep reflexes, dilatation of pupils, and slight ataxia. Euphoria occurring in outbursts was prominent. Increased accessibility and amiability, with increased release of libido and greater accessibility of delusional material was observed in addition to visual hallucinatory experiences (Forrer and Goldner).⁵⁷ Hoch⁹⁴ describes the effect of intravenous injection of synthetic mescaline on a group of schizophrenic patients and on "normal" voluntary controls. The effects, lasting 10 to 20 hours, were exhibited in such physical signs as pallor or flushing, restlessness, dilated pupils, impairment in pain sensation, spatial discrimination, and body orientation, tremor and incoordination. Psychiatric manifestations occurred in a state of clear consciousness. Visual hallucinations filled with condensations, symbolizations, and wish-fulfilling fantasies, auditory hallucinations, somatic sensation, paranoid, grandiose or hypochondriacal delusions, misinterpretation of environmental situations, depersonalization experiences, incoherence, flight of ideas, blocking and speech disorders, motor disturbances, depression or euphoria, anxiety and fear were often observed. Mescaline was able to underscore the schizophrenic symptoms of patients and was able to precipitate schizophrenic psychosis in persons suffering from latent schizophrenia, and to reactivate the psychosis in patients who had improved after psychosurgery, although in these patients their response to the drug was quantitatively less conspicuous than before.

The symptoms caused by mescaline, hashish, cocaine, lysergic acid, and even amphetamine, all belong to the large group of exogenous reactions of which delirium is the typical form. Differences in symptoms found with various drugs have been attributed to differences in the personality of the subjects, but each drug does show certain special features. Mescaline produces derealization, followed by visual and tactile illusions in relative clearness of the sensorium; hashish produces special forms of dissociation of thought, with hyperkinesis; cocaine produces mainly auditory hallucinations, with fear, increasing to terror, often with a sexual coloring. The symptoms of lysergic acid appear to be closest to those of mescaline, though its chemical nature differs widely. The mechanism by which mental symptoms are produced by these drugs remains to be clarified (Mayer-Gross).¹³³

GERIATRICS

The problems of geriatrics and gerontology are receiving increasing attention in many medical fields. These are well summarized by Shock¹⁸⁹ who discusses the trends in population change, employment and retirement policies for the elderly, difficulties in health, maintenance, living arrangements, etc. He has also prepared a classified bibliography on gerontology and geriatrics.¹⁹⁰ The importance of rehabilitation in the aged is emphasized by Rusk¹⁷² who recommends further research into the causes of degenerative diseases and the aging process, a program of prevention, improvement in methods of definitive medical and surgical care, and a program aimed at rehabilitation and utilization of the chronically ill and disabled. The sociologic changes occasioned by the aging of the population cut deep into the social pattern of every community, society's response to these lagging far behind the recognized indications for action (Randall,¹⁶¹ Moore¹⁴³).

Kaplan¹⁰³ deplores the fact that biologists and psychologists have concentrated their attention on the abnormal to the neglect of the study of the healthy well adjusted individuals over 70. He recommends longitudinal as well as cross sectional studies of the aged, and that batteries of biologic and psychologic tests be devised to determine true biologic age in contrast to chronologic age. By studying the differential rates of psychoses of the aged in co-twin, siblings and parents in a series of 3,205 twin index cases, with and without psychosis, Kallmann¹⁰¹ has demonstrated that psychoses occur more frequently among the blood relatives of the psychotic index cases than in those without psychoses.

In his discussion of the sexual functions in the aging male, Stokes²⁰⁴ emphasizes that in present culture there is a definite trend toward early loss of potency. When anxiety and guilt reactions are not great, the male may remain quite potent. In fact, the young quickly-ejaculating male is more apt to become impotent early. Older men who show aggressive sexual interest in young girls generally have a life-long history of similar reactions.

Freyhan et al.⁶¹ studied cerebral blood flow and cerebral metabolism in patients diagnosed as senile psychosis and psychosis with cerebral arteriosclerosis, and conclude that these psychoses are associated with and probably are the result of a significant reduction in cerebral oxygen utilization on the basis of an increased cerebrovascular resistance, and the resultant significant reduction in blood flow through the brain. These diseases are in striking contrast to schizophrenia in which no circulatory or metabolic deviation from the normal was observed. A correlation between electroencephalographic abnormalities and the degree of organic mental impairment was observed by Luce and Rothschild.¹²⁸

A type of grief reaction in the elderly is described by Stern et al.²⁰¹ This

is characterized by a relative paucity of overt grief and of conscious guilt feelings, a preponderance of somatic illness precipitated by bereavement, a tendency to exaggeration of the idealization of the deceased with a blotting-out of all "dark features," a tendency to self isolation, and to hostility against some living person. The major therapeutic emphasis was on manipulation of the environment and interpretation to the relatives. Psychiatric aspects of aging are discussed by Himler⁸⁸ and Simon¹⁹⁸ who emphasize that there must be a greater appreciation of the need for the aged to continue useful interests and activities if they are to maintain an adequate social life and a useful place in the community. A series of 35 suicides and attempted suicides is described by Kioerboe¹⁰⁶ who gives physical discomfort, chronic alcoholism, syphilis, and mental changes as principal motives.

For the most part, administration of steroid hormones is found to have a favorable therapeutic effect on aging people. Kirk¹⁰⁷ reports that testosterone increases muscular strength, alleviates feelings of depression and improves sexual potency in aging males, while estrogen relieves many of the post menopausal complaints in women. Forster⁸⁸ treated nine cases of senile and arteriosclerotic dementia by daily injections of cytochrome C and gave nine similar cases injections of normal saline, and it was not possible to demonstrate any significant improvement in the treated group over the controls. Gottlieb and Morris⁷⁹ confirm that aged depressed patients with evidence of osteoporosis or osteomalacia may undergo electroshock therapy safely if curarization technics are used, and Robinson¹⁶⁸ reports on the successful electroshock treatment of patients over 80 suffering from depression.

It has been recommended that a new set of principles may be necessary before the overage adult can be educated effectively to cope with problems of his specific concern. In general, industry has not been properly motivated to adequately analyze the problem of the aged (Scheid).¹⁷⁹ Proposals to keep older people in the nation's manpower pool as productive members include the establishment of a retirement panel to review each worker coming up for retirement, rehabilitation of workers with chronic disease, and the early detection and prevention of disease by means of periodic examinations (Franco).⁶⁹

According to Tompkins,²¹² adequate hospital care of the aged requires a psychiatrist and an occupational therapist for every 100 patients, a graduate nurse for every 20, and an aide for every 12. The home care plan developed by Montefiore Hospital, New York City, is proving successful in providing adequate medical care, reducing expenses, keeping the family unit intact and releasing scarce hospital beds.

That dementia in seniles may be caused by a variety of disease entities

is emphasized by Fisher.⁵⁵ He describes a case of severe senile dementia in which post-mortem examination uncovered a previously unsuspected lesion—complete occlusion of the cervical portion of both internal carotid arteries. Carotid arteriography is the only method of making the diagnosis in life, although in addition to carotid disease there are usually signs of widespread atherosclerosis.

MILITARY AND CIVILIAN DEFENSE PSYCHIATRY

Military. Lessons learned in World Wars I and II throw considerable light upon the various problems which the military psychiatrist may encounter and a large body of data concerning the problem of selection and screening methods, methods of training, the role of leadership and group affiliation, as well as physiologic, pharmacologic and psychologic methods of moderating the severity of the stress which military personnel may encounter is being documented. Although much of the information available has to do with the "symptomatic" approach to problems, the real advances in military psychiatry will come only when everyone recognizes that the forces collectively called "motivation" and "morale" are the most important psychologic elements of military life. An informed citizenry is the best bulwark against the corrosive inroads of psychologic insecurity. The symptoms of stress in the body politic are homologues of the anxieties, dissatisfactions and behavioral disturbances which the military psychiatrist treats in his practice. The job of the military psychiatrist will be greatly lightened if the immunizing effect of good training, morale and motivation, and of over-all preparation for the stress of combat is constantly kept in mind. (Braceland²⁶).

The value of the brief psychiatric interview in screening possible future psychiatric casualties in military life has been questioned by many, but Wittson and Hunt,²²⁶ after a study of 944 cases of naval personnel, interviewed because of suspected neuropsychiatric symptomatology, believe that the brief interview is valid as a classificatory procedure. They divided the group studied on the basis of a brief psychiatric interview into three classes: those with mild symptoms and no treatment; moderate symptoms and shore duty; and severe symptoms and hospitalization. The subsequent naval careers of these men were studied for one year. The neuropsychiatric discharge rates for the three groups were in accord with the original prediction. The mild group lost 6.5 per cent for neuropsychiatric reasons, the moderate 20.2 per cent, and the severe group 89.7 per cent.

The follow-up data for a period of five to eight years on 100 patients with schizophrenia or schizophrenic-like reactions occurring in a combat area were investigated by Ripley and Wolf.¹⁶⁶ The study revealed that there was a high incidence of psychopathologic symptoms prior to the illness

developing overseas, and that the most common precipitating factors appeared to be traumatic incidents in combat, family problems, sexual conflicts, prolonged overseas service, difficulty in accepting responsibility, dissatisfaction with the army assignment, and problems in interpersonal relationships with others in the organization. Eighty per cent of the patients were evacuated to the United States within two months of hospitalization and, on reaching the United States, one-fifth had shown marked symptomatic improvement, and after two months of hospitalization over one-third of the patients had been discharged, while only four were continuously hospitalized for more than one year. There was a gradual trend toward decrease in disability as time went on, though the personality deviations characteristic of the schizophrenic process persisted, and after five or more years severely handicapping symptoms were still present in one-fifth of the patients. The long term course of the patients studied indicated, despite previous reports, that schizophrenia in the military service does not differ essentially from that occurring in civilian life, and that some schizophrenics function in the army for long periods prior to the acute episode despite psychologic symptoms. It was concluded that vulnerability in civilian life indicated that such individuals should not be accepted for military duty; a policy of returning soldiers to the United States after a definite period of service overseas may be of use in decreasing the number of psychiatric casualties; the physician with an understanding of psychiatry may be of great help in preventing and treating psychiatric casualties; and there has been too much emphasis on granting disability compensation and too little on rehabilitation.

Although approximately 50 per cent of a representative sample of enlisted men with psychoneurotic disorders during World War II had significant and clinically recognizable psychiatric difficulties prior to entering the service, the remainder were sufficiently well adjusted so that they could not have been rejected for induction under any conceivable screening examination. (Brill and Beebe²⁷). Even the group with overt neuroses prior to entering the service was by no means a total loss, as, in 18 per cent, breakdown did not occur except under the stress of combat; 32 per cent served overseas; and 30 per cent were demobilized without requiring a medical discharge. It was estimated that about 60 per cent of those who received disability discharge were capable of working full time in some capacity at the time of separation. At the time of follow-up, only 8 per cent were severely or totally disabled, although 47 per cent were receiving disability compensation. The condition of more than half of the men has improved since separation, but most of those who were severely disabled at follow-up had become worse since separation. The majority of those who were severely or totally disabled at follow-up had some difficulty

prior to service. The severity and duration of combat were not related to the degree of disability and there was a suggestion that discharge for disability in itself may contribute to the perpetuation or aggravation of psychoneurotic disorders. A summary of experiences with a large group of cases of traumatic war neuroses during the five-year period since the end of the war is reported by Futterman and Pumpian-Mindlin.⁶⁴ Traumatic war neuroses occurred in noncombatant military personnel located in a combat area with a relatively high degree of frequency because these people were exposed to traumata without the possibility of effective motor discharge of the emotions thereby engendered. Guilt about killing or assailing defenseless enemy personnel, either military or civilian, is an important factor in the precipitation of a traumatic war neurosis since the superimposed military code yields to the earlier and stronger civilian prohibition against violence toward others. Traumatic war neurosis often occurs in conjunction with physical injury because separation from the unit, as a result of physical injury, removes the influence of group moral. Physical injury or medical or surgical disorder that leads to enforced immobilization encourages the development of the traumatic war neurosis by depriving the individual of the possibility of discharge of tension through any other motor activity. The monotonous repetition of the traumatic war experience and combat dreams in these cases is caused by the transformation of the world into a threatening place, changes in the details of the repetitive traumatic experiences and combat dreams being significant indicators of the points at which the traumatic are linked with pretraumatic experiences. The authors do not believe that the use of intravenous narcosis or hypnosis has been particularly helpful to this group.

The psychopathology of a group of 1800 patients who reacted to the isolated situation of a combat zone in the Southwest Pacific was studied by Ripley and Wolf.¹⁶⁵ An unusually large number of patients had had disturbed early environmental backgrounds and a high incidence of family emotional disorders. Those who gave evidence of having a fairly stable adjustment in civil life were less susceptible to schizophrenia and more likely to develop a reactive depression or anxiety state when they did decompensate. Those from rural areas were more likely to develop schizophrenia. The patients who had experienced psychopathologic reactions during combat were prone to develop a revival of symptoms prior to or on return to fighting, and in many there was a reactivation of illness which had previously appeared in civilian life. The incidence of personality disorders were appreciably higher in Negro than among white groups. Psychopathic personalities were found to be particularly susceptible to neurotic and psychotic illnesses under circumstances of feeling trapped by the restrictions and discipline of Army life. Many patients with neurotic syn-

dromes early in the course of their illness later developed disorganizing psychosis.

The unusual situation of isolation from women made the sexual reactions of the men noteworthy. As would be expected, there was a high incidence of masturbation and homosexuality, and on return to contact with women, both excessive heterosexuality and impotence were frequent. When the diet was unappetizing or deficient, preoccupation with food became marked and took precedence over thoughts about sex. Good morale, sustained by pride in the organization, respect for officers and fellow soldiers, confidence in equipment, the feeling of being properly trained, high quality of food and recreational outlets were influences in preventing illness or lowering its incidence. The study by Egan et al.⁴⁵ of 2,054 men originally rejected for neuropsychiatric reasons, who later served in the army, indicates that a large number of rejectees could have served profitably in some capacity and would have been discharged honorably and without neuropsychiatric disability. Seventy-nine and four-tenths per cent of this group gave satisfactory service. The authors recommend that determination under observation within the Armed Forces rather than by screening at the induction station should be made concerning any man's usefulness. After it is determined that he cannot be used profitably, he should be discharged without any obligation to the government because of so-called aggravation. This conclusion is concurred in by Klein.¹⁰⁸

In an excellent review on Military Medicine in the Far East Command, a group of army officers—Glass,⁶⁹⁻⁷³ Kolansky and Cole,¹¹³ Bolocan,²² Caveness and Perry,³² Caveness and Allen,³⁰ Caveness and Christensen,³¹ Blacher,¹⁷ Mariner¹³¹ and Jacobson⁹⁷ discuss the following: field hospital neuropsychiatric service, combat exhaustion, division psychiatry, the transition from civil to combat psychiatry, states of altered consciousness, blast concussion, the medical evaluation of the noneffective soldier, outpatient psychiatry in an overseas theater, brief psychotherapy of the war neuroses, psychiatric treatment in the environment of an overseas convalescent hospital, and the problems of medical evacuation and the gain in illness.

Civilian Defense. An action program concerning the psychiatric aspects of civilian defense has been suggested by Fantl⁵⁰ who recommends that this should include control of panic, the prevention of persistent psychiatric disorders due to exposure to bombing, the prevention of psychiatric disorders in children who are evacuated or separated from their parents, the care of the aged, and the continuation and expansion of an effective and practical peacetime preventive psychiatric program. The author emphasizes that in England during World War II panic presented a much smaller problem than was expected, and that in Japan there was no panic until the

atom bomb was used. To prevent panic, the public must be educated and a master plan developed which should help each individual find an active place in the total defense program. After the disaster strikes, there must be a known reliable information source, mobile facilities for taking care of acute psychiatric casualties, uniformed civilian defense members, mobile kitchens, mobile laundry units and availability of welfare agencies. The experience in England during the last war indicated that there were more psychiatric disturbances among the evacuated children than among the bombed children. Children under two reacted primarily to the mother's feeling of calm or fear. Those two to five reacted better if their mothers were with them and if their mothers were calm. School children did better if their class unit was kept intact. The reaction of children was largely determined by the suddenness of separation from the parents, suddenness of change to a new environment and new adults, and the type of placement and organization. One of the main difficulties in the handling of the aged was their reluctance to change and their slowness which interfered with rescue operations. Details of a first aid program in the handling of acute panic states are given by Meerloo.¹³⁶ Even if a population is well prepared and has a good morale, people will be overcome by fear temporarily, but in a well organized defense system, mass panic can be prevented. Paradoxically enough, fear reactions may be seen after the panic is passed. Two different types of panic behavior are observed: a general paralysis characterized by apathy, mutism, and immobility, a type of cataleptic reaction which might have a frightening influence on bystanders; and temper tantrums, in which the individual might behave like an angry child. The program recommended by the author is as follows: a paternal, understand attitude on the part of the therapist; no narcotics or sedatives; "oral satisfaction" in the form of hot coffee, soup, or cigarettes; "first-aid hypnosis"; and "first aid catharsis."

Tyhurst²¹⁴ describes three overlapping phases in reaction to a community disaster: a period of impact of initial stress; a period of recoil characterized by a suspension of the initial stress when the individual has succeeded in avoiding this direct effect, for the moment at least, by one maneuver or another; and a post-traumatic period which is more obviously "social" in nature, during which there is an awareness of what the disaster means in terms of loss of home, financial security, and bereavement. To determine psychologic reactions to severe chronic stress, Kral¹¹⁵ studied the reactions and behavior of the internees in an internment camp. Every internee suffered an initial phase of reactive depression. The life and conditions in the camp did not appear to influence endogenous psychoses, and no new cases of psychoneurosis originated in the camp. In fact, old and lasting conditions of that kind improved, although after liberation such

neurotic reactions were sometimes reactivated. Libuse Tyhurst²¹⁵ studied 48 displaced persons and immigrants in the area of Montreal. He describes two characteristic periods through which these people go, the first lasting about two months with characteristics of a sense of well-being and euphoria, with primary interest directed toward the fulfillment of basic needs like food and sleep, and a tendency to ventilate about their war experiences. The second period he calls the "period of psychological arrival," during which the individual becomes increasingly aware of the language difficulties, differences in customs, separations and losses, and is concerned with the distant past which is retrospectively idealized. The three main trends in the clinical pictures which developed were suspiciousness and paranoid trends; anxiety and depression, and somatic complaints. The social factors were felt to be most important in the development of these symptom patterns, the social patterns operating horizontally as the individual moved from one culture to another, and vertically as he moved from one social class to another. The psychologic consequences of such change lead to increasing isolation, personal insecurity, reorientation of values, failing communication, insecurity, and anxiety.

Meerloo¹³⁵ asks the question, "By what means are bitter opponents of a regime brought to their knees, not only to confess to crimes against the existing order, but even to support its ideology, to reverse their former political attitudes? What goes on behind the closed doors of the interrogation chamber? More importantly, what goes on in the minds of such victims?" He calls the organized system of psychologic intervention and judicial perversion, in which a powerful tyrant synthetically injects his own thoughts and words into the minds and mouths of the victims he plans to destroy by mock trial, menticide. This is done in three phases. The first phase is directed toward extorting confession, and during this the victim is bombarded with questions for days and nights, is inadequately fed and is allowed no rest while his inquisitors take turns with him. He is pursued by the unsteadiness of his own mind, which cannot always produce the same answer to the same question. He is pursued by hidden guilt feelings that undermine his rational awareness of innocence. He is pursued by a need for companionship. From within and without he is inexorably driven toward signing the confession prepared by his persecutors. The second phase trains the victim to accept his own confession. False admissions are repeated and hammered into his brain; he is forced to reproduce fictitious details that ultimately convince him of his criminal status. He is in a state of autohypnosis in which he convinces himself of fabricated crimes. In the third phase, the victim completely conditioned and accepting his own guilt, is trained to bear false witness against himself; he is prepared for trial, completely softened, remorseful, and willing to be sentenced. The

author recommends that by calling international attention to this evil, and by dignifying it with a name, mankind will be able to fight against it when the United Nations will devise rules for curtailing this form of psychologic attack.

HOSPITAL ADMINISTRATION

The proceedings of the Second Mental Hospital Institute held under the auspices of the Mental Hospital Service of the American Psychiatric Association, 1950, are now available in written form. They cover such areas of interest as hospital architecture, inspection and rating, the role of the hospital in civil defense, day hospitals, group therapy, hospital-community relationships, etc.¹³³ Bane¹⁰ reports on the Governor's Study on Mental Hospitals which states emphatically that the 202 State hospitals for the mentally ill are overcrowded. He recommends that modern equipment be installed, buildings modernized, number of personnel, teaching and training facilities, and research programs be expanded. In letters to the editor, Lemkau¹²⁰ recommends that programs of mental hygiene be integrated through public health officers wherever possible, while Russell¹⁷³ considers that such an attitude in the present stage of psychiatry and mental hygiene education and practice is premature and unrealistic. The Central Inspection Board of the American Psychiatric Association has developed a graphic method of presenting the functional efficiency or evaluation of a mental hospital in the form of a profile which should prove an effective tool for public education with regard to the mental hospitals in the United States and Canada. (Chambers et al.³³). The future organization of psychiatric care is outlined by Lemkau¹²¹ who believes we must avoid the dangerous generality of "mental disease" and recognize the concept of multiple etiology at various integrative levels. In his opinion, the non-medical responsibilities of psychiatrists will be removed from them more and more, and physicians will no longer need to pass as both therapists and businessmen.

The major difference in the point of view of a hospital administrator and a psychiatrist is that the administrator's point of view is group centered rather than individual centered. Sheffel¹⁸⁸ emphasizes some concepts useful to administrators: (a) administration is concerned with people not paper; (b) duties and responsibilities should be clearly defined; (c) conservation of organization energy is a problem of administration; (d) the equilibrium of the organization is constantly threatened; (e) communication systems require continuous attention. Baganz¹¹ emphasizes that efficient administration has three primary functions: deputizing, authorizing and supervising. Deputizing and authorizing require little but the initial action, but the problem of the hospital administrator is the problem of efficient

and appropriate supervision, and for this there must be clear and free flow of information from the top levels of management to the individual at the operating level.

The authoritative function of psychiatric hospitals and psychotherapists have many psychotherapeutic implications (Worden²²⁷). The policy of a psychiatric hospital should restrict the patient's activity to the hospital program and increased freedom should be viewed not only in regard to potential danger but also in regard to how such freedom can serve a therapeutic goal. By this experience in relation to authority, the patient may bring to expression distorted attitudes regarding authority and have an opportunity to develop a new orientation to this fundamental fact of social living. In some hospitals, two physicians are assigned to a patient, one to serve the authoritative (bad) function and one to serve the psychotherapeutic (good) function. Such a separation is often the result of the physician's anxiety rather than of the patient's need. This device has the disadvantage that the patient suspects, sometimes correctly, that the therapist merely pretends to assign authority to the administrative physician so as to escape responsibility. If the therapist really tried, he could get the administrative physician to write whatever orders he wanted. (Kohl¹¹²).

Kaldeck¹⁰⁰ describes the successful use of nurses and attendants as group leaders in a large group therapy program conducted in a mental hospital with a minimum of trained psychotherapists. The persons selected as leaders were given lectures and instructions as to technic and the supervising physician met with them once a week to report on their experiences and discuss problems which had come up. As a result, patients have displayed considerable improvement, the attendants have grown in ability and self-esteem, and a therapeutic rather than a custodial attitude has permeated the hospital.

An effort was made at better selection and placement of psychiatric aides by Yerbury et al.,²²⁹ but the psychologic tests utilized (Revised Beta Examination and Multiple Choice Rorschach) could only distinguish between those that were very good and those that were very poor. Increasing efforts are being made by many hospitals to bring the community into the hospital and to extend the hospital into the community. Sewall et al.¹⁸⁷ emphasize that the hospital has a responsibility to make proper vocational replacement when a patient is discharged. Volunteer workers may be of great aid in amplifying the hospital program, but this depends on the hospital assuming responsibility for supervising and programming volunteer activities. (Fechner and Parke,⁵² Haddock and Dundon⁸⁰).

Felix⁵⁴ comments on the draft act suggested by the Federal Security Agency as an aid to State legislatures in drafting new laws for the hospitalization of the mentally ill. The draft act seeks to provide three basic

assurances: (1) maximum opportunity for prompt medical care; (2) protection against emotionally harmful experiences; (3) protection against unwarranted confinement.

Muncie and Billings¹⁴⁶ made a survey of information relevant to the private practice of psychiatry in the United States and Canada. The average age of a psychiatric practitioner is 41 years. The majority have been in practice less than 10 years; two out of every three are diplomates of the American Board; most are practicing in big cities and practice "general psychiatry," and the majority participate in teaching programs. The inadequacy of present psychiatric facilities in general hospitals is stressed by Bennett et al.¹⁴ How increasing the number of psychiatric units in general hospitals may help in improving the care of the mentally ill is described by Gayle.⁶⁷

Tuberculosis continues to be a serious problem in mental hospitals and its control rests on planned, orderly case finding methods. Patients with proved active disease and those in whom activity is suspected should be segregated in special wards or buildings (Wassersug and McLaughlin²²⁰). How such a program was carried out in New York State is described by Katz.¹⁰⁴

REFERENCES

- ¹ Aarons, Z. Alexander: Some aspects of theory and treatment of schizophrenia. *Psychoanalyt. Rev.* 38:113, 1951.
- ² Albee, George W.: Prognostic importance of delusions in schizophrenia. *J. Abnorm. & Social Psychol.* 46:208, 1951.
- ³ Alexander, E. J.: Withdrawal effects of sodium amytal. *Dis. Nerv. System.* 12:77, 1951.
- ⁴ Alexander, Leo: Element of psychotherapy in the treatment of organic neurologic disorders. *J. Nerv. & Ment. Dis.* 114:283, 1951.
- ⁵ Altschule, Mark D.: Effects of factors that modify cerebral blood flow on hallucinations in schizophrenia. *J. Clin. & Exper. Psychopath.* 12:123, 1951.
- ⁶ —, Siegel, Elaine, and Mora-Castaneda, Federico: Significance of rise in blood sugar level after injection of epinephrine in mental disease. *Arch. Neurol. & Psychiat.* 65:589, 1951.
- ⁷ Apter, Nathaniel S. and Halstead, Ward C.: Impaired cerebral functions in essential hypertension. *Am. J. Psychiat.* 107:808, 1951.
- ⁸ Arnow, Aron J.: Influence of an intense transference on a schizophrenic patient. *Bull. Menninger Clinic* 15:100, 1951.
- ⁹ Asher, Richard: Münchausen's syndrome. *Lancet.* 1:339, 1951.
- ¹⁰ Bane, Frank: Governors' study on mental hospitals. *Ment. Hyg.* 35:10, 1951.
- ¹¹ Baganz, Crawford N.: Psychiatric aspects of hospital administration. *Am. J. Psychiat.* 108:277, 1951.
- ¹² Bartemeier, Leo H.: Psychiatry and international understanding. *Am. J. Psychiat.* 107:641, 1951.
- ¹³ Bateman, J. Fremont and Papez, James W.: Significance of the thalamus in psychoses. *J. Clin. & Exper. Psychopath.* 12:89, 1951.

- ¹⁴ Bennett, A. E., Hargrove, Eugene A., and Engle, Bernice: Present status and future needs of psychiatric facilities in general hospitals in the United States and Canada. *Am. J. Psychiat.* 108:321, 1951.
- ¹⁵ Binger, Carl: Public education in psychiatry. Is it possible? Is it desirable? *Am. J. Psychotherapy.* 5:4, 1951.
- ¹⁶ Bingham, June: What the public thinks of psychiatry. *Am. J. Psychiat.* 107:599, 1951.
- ¹⁷ Blacher, Richard S.: Psychiatric treatment in the environment of an overseas convalescent hospital. Symposium on Military Medicine in the Far East Command, a Supple. issue: The surgeon's circular letter, Medical Section 120, Sept. 1951.
- ¹⁸ Bleuler, Manfred: Psychopathology of acromegaly. *J. Nerv. & Ment. Dis.* 113:497, 1951.
- ¹⁹ Blom, Gaston E.: Review of electrocardiographic changes in emotional states. *J. Nerv. & Ment. Dis.* 113:283, 1951.
- ²⁰ Bockoven, J. Sanbourne, Greenblatt, Milton, and Solomon, Harry C.: Treatment results in the major psychoses. *New England J. Med.* 244:357, 1951.
- ²¹ Boisen, Anton T.: Development and validation of religious faith. *Psychiatry.* 14:455, 1951.
- ²² Bolocan, Hyman: Division Psychiatry. Symposium on Military Medicine in the Far East Command, a Suppl. issue: The surgeon's circular letter, Medical Section, 109, Sept. 1951.
- ²³ Bonner, Hubert: Problem of diagnosis in paranoic disorder. *Am. J. Psychiat.* 107:677, 1951.
- ²⁴ Borberg, William: On methods of the social sciences in their approach to international problems. *Am. J. Psychiat.* 107:650, 1951.
- ²⁵ Bowman, Karl M. and Rose, Milton: Criticism of the terms "psychosis," "psycho-neurosis," and "neurosis." *Am. J. Psychiat.* 108:161, 1951.
- ²⁶ Braceland, Francis J.: Military psychiatry today. *Ann. Int. Med.* 35:432, 1951.
- ²⁷ Brill, Norman Q. and Beebe, Gilbert W.: Follow-up study of psychoneuroses. *Am. J. Psychiat.* 108:417, 1951.
- ²⁸ Brown, G. Gordon: Culture, society and personality: A restatement. *Am. J. Psychiat.* 108:173, 1951.
- ²⁹ Bullock, F. N., Clancey, I. W., and Fleischhacker, H. H.: Studies in schizophrenia. *J. Ment. Sc.* 97:197, 1951.
- ³⁰ Caveness, William F. and Allen, James N.: States of altered consciousness (fits and faints). Symposium on Military Medicine in the Far East Command, a Suppl. issue: The surgeon's circular letter, Medical Section 135, Sept. 1951.
- ³¹ Caveness, William F. and Christensen, Norman M.: Blast concussion. Symposium on Military Medicine in the Far East Command, a Suppl. issue: The surgeon's circular letter, Medical Section 134, Sept. 1951.
- ³² Caveness, William F. and Perry, Donald J.: Headache. Symposium on Military Medicine in the Far East Command, a Suppl. Issue: The surgeon's circular letter, Medical Section, 138, Sept. 1951.
- ³³ Chambers, Ralph M., Tarumianz, Mesrop A., and Appel, Kenneth E.: Profile of hospital functioning. *Am. J. Psychiat.* 108:271, 1951.
- ³⁴ Cohn, Jay B., Karnosh, Louis J., and Stecher, Robert M.: Clinical trials with cortisone in the treatment of chronic schizophrenia. *Dis. Nerv. System* 12:291, 1951.

- ³⁵ Colby, Kenneth Mark: Primer for psychotherapists. New York, Ronald Press Co., 1951.
- ³⁶ Comment: Gobbledygook in psychiatric writing. *Am. J. Psychiat.* 108:474, 1951.
- ³⁷ Corsellis, J. A. N.: Sub-acute sclerosing leuco-encephalitis: a clinical and pathological report of two cases. *J. Ment. Sc.* 97:570, 1951.
- ³⁸ Darr, George C. and Worden, Frederic G.: Case report twenty-eight years after an infantile autistic disorder. *Am. J. Orthopsychiat.* 21:559, 1951.
- ³⁹ Delgado, Honario and Carrillo-Broatch, Andres: Treatment of depression and agitation with desoxyephedrine hydrochloride. *Rev. neuro-psiquiat.* 13:539, 1950.
- ⁴⁰ Doll, Edgar A.: Neurophrenia. *Am. J. Psychiat.* 108:50, 1951.
- ⁴¹ Drubin, Lester and Singer, Martin: Diagnosing mental deficiency in psychotics. *Am. J. Psychiat.* 108:138, 1951.
- ⁴² Duhl, Leonard J.: Effect of baby bottle feedings on a schizophrenic patient. Case report. *Bull. Menninger Clinic* 15:21, 1951.
- ⁴³ Eaton, Joseph W.: Assessment of mental health. *Am. J. Psychiat.* 108:81, 1951.
- ⁴⁴ — and Weil, Robert J.: Psychotherapeutic principles in social research. *Psychiatry*. 14:439, 1951.
- ⁴⁵ Egan, John R., Jackson, Lionel, and Eanes, Richard H.: Study of neuropsychiatric rejectees. *J.A.M.A.* 145:466, 1951.
- ⁴⁶ Ehrmann, Howard M.: Contribution of history to international understanding. *Am. J. Psychiat.* 107:657, 1951.
- ⁴⁷ Eisenstein, Victor W.: Differential psychotherapy of borderline states. *Psychiatric. Quart.* 25:379, 1951.
- ⁴⁸ Eissler, K. R.: Remarks on the psycho-analysis of schizophrenia. *Internat. J. Psycho-Analysis.* 32:139, 1951.
- ⁴⁹ El Kholy, M. K.: Crime in the psychoses complicating pellagra. *J. Ment. Sc.* 97:191, 1951.
- ⁵⁰ Fantl, Kurt: Psychiatric aspects of civilian defense. *Am. J. Psychiat.* 107:488, 1951.
- ⁵¹ Farrar, Clarence B.: Suicide. *J. Clin. & Exper. Psychopath.* 12:79, 1951.
- ⁵² Fechner, A. H., and Parke, James H.: Volunteer worker and the psychiatric hospital. *Am. J. Psychiat.* 107:602, 1951.
- ⁵³ Feldman, Marvin J. and Drasgow, James: A visual-verbal test for schizophrenia. *Psychiatric. Quart. Suppl.* 25:55, 1951.
- ⁵⁴ Felix, R. H.: Comment: hospitalization of the mentally ill. *Am. J. Psychiat.* 107:712, 1951.
- ⁵⁵ Fisher, Miller: Senile dementia—a new explanation of its causation. *Canad. M. A. J.* 65:1, 1951.
- ⁵⁶ Forrer, Gordon R.: Atropine toxicity in the treatment of mental disease. *Am. J. Psychiat.* 108:107, 1951.
- ⁵⁷ — and Goldner, Richard D.: Experimental physiological studies with lysergic acid diethylamide (LSD-25). *Arch. Neurol. & Psychiat.* 65:581, 1951.
- ⁵⁸ Forster, W.: Cytochrome C in senile and arteriosclerotic dementia. *J. Ment. Sc.* 97:718, 1951.
- ⁵⁹ Franco, S. Charles: Industrial medical aspects of aging. *J.A.M.A.* 147:1328, 1951.
- ⁶⁰ Freeman, John G. and Kolb, Lawrence C.: Acute intermittent porphyria: associated psychiatric symptoms treated by electroshock. *Proc. Staff Meet., Mayo Clin.* 26:401, 1951.

- ⁶¹ Freyhan, F. A., Woodford, R. B., and Kety, Seymour S.: Cerebral blood flow and metabolism in psychoses of senility. *J. Nerv. & Ment. Dis.* 113:449, 1951.
- ⁶² Friedlander, J. H.: Comments on the relationship of the responsivity of the adrenal cortex and schizophrenia. *Psychiatric Quart. Suppl.* 25:76, 1951.
- ⁶³ Funkenstein, Daniel H., Greenblatt, Milton, and Solomon, Harry C.: Autonomic changes paralleling psychologic changes in mentally ill patients. *J. Nerv. & Ment. Dis.* 114:1, 1951.
- ⁶⁴ Futterman, Samuel and Pumpian-Mindlin, Eugene: Traumatic war neuroses five years later. *Am. J. Psychiat.* 108:401, 1951.
- ⁶⁵ Galdston, Iago: Psychiatry without Freud. *Arch. Neurol. & Psychiat.* 66:69, 1951.
- ⁶⁶ Garcia, J. Alves: Theorie affective des hallucinations. *Ann. med.-psychol.* 109:170, 1951.
- ⁶⁷ Gayle, R. Finley, Jr.: Role of the general hospital in the care of the mentally ill. *Am. J. Psychiat.* 108:103, 1951.
- ⁶⁸ Glaser, Gilbert H. and Hoch, Paul H.: Observations on effect of corticotrophin in schizophrenia. *Arch. Neuro. & Psychiat.* 66:697, 1951.
- ⁶⁹ Glass, Albert J.: From civil to combat psychiatry. Symposium on Military Medicine in the Far East Command, a Suppl. issue: The surgeon's circular letter, Medical Section 105, Sept. 1951.
- ⁷⁰ —: Medical evaluation of the non-effective officer. Symposium on Military Medicine in the Far East Command, a Suppl. issue: The Surgeon's circular letter, Medical Section, 129, Sept. 1951.
- ⁷¹ —: Combat exhaustion. Symposium on Military Medicine in the Far East Command, a Suppl. Issue: The Surgeon's circular letter, Medical Section, 112, Sept. 1951.
- ⁷² —: Medical evacuation and the gain in illness. Symposium on Military Medicine in the Far East Command, a Suppl. issue: The Surgeon's circular letter, Medical Section, 118, Sept. 1951.
- ⁷³ —: Combat exhaustion. *U.S. Armed Forces M. J.* 2: 1471, 1951.
- ⁷⁴ Goldfarb, Walter and Park, Paul D.: Dynamic role of group therapy in the total treatment program of psychotic patients. *Am. J. Psychotherapy.* 5:514, 1951.
- ⁷⁵ Goldner, Richard D. and Forrer, Gordon R.: Alteration of accessibility with scopolamine. *Dis. Nerv. System* 12:213, 1951.
- ⁷⁶ Gordon, Alfred: Precipitating factors in neuroses and psychoses. *A.M.A. Arch. Neurol. & Psychiat.* 66:571, 1951.
- ⁷⁷ Gottesfeld, Benjamin H., Lasser, Leonard M., Conway, Edward J., and Mann, Norman M.: Psychiatric implications of the treatment of alcoholism with tetraethylthiuram disulfide. *Quart. J. Stud. on Alcohol* 12:184, 1951.
- ⁷⁸ Gottfried, Sidney P. and Minsky, Isadore: Studies on excretion of total neutral 17-ketosteroids in schizophrenic patients. *Arch. Neurol. & Psychiat.* 66:708, 1951.
- ⁷⁹ Gottlieb, J. S. and Morris, L. E.: Electric convulsive therapy with complete curarization. *J. Gerontol.* 6:92, 1951.
- ⁸⁰ Haddock, James N. and Dundon, H. Dwyer: Volunteer work in a state hospital by college students. *Ment. Health.* 35:599, 1951.
- ⁸¹ Hall, K. R. L.: Testing of abstraction, with special reference to impairment in schizophrenia. *Brit. J. M. Psychol.* 24:118, 1951.
- ⁸² Harris, A.: Treatment of depression by dinitrile succinate. *J. Ment. Sc.* 97:209, 1951.

- ⁸³ Hauser, A., Beyer, Alvin Jr., and Burger, Robert A.: Encephalopathy associated with acute diffuse platelet thrombosis, report of a case. *Arch. Neurol. & Psychiat.* 65:672, 1951.
- ⁸⁴ Hecker, Arthur O., Mercer, Margaret, and Griffin, Mark A., Jr.: Further clinical investigation of tolserol (myanesin). *Dis. Nerv. System* 12:99, 1951.
- ⁸⁵ Hendin, Herbert: Psychodynamic motivational factors in suicide. *Psychiatric Quart.* 25:672, 1951.
- ⁸⁶ Hill, Denis, Loe, P. St. J., Theobald, J., and Waddell, Marion: Central homeostatic mechanism in schizophrenia. *J. Ment. Sc.* 97:111, 1951.
- ⁸⁷ Hillbom, Eero: Schizophrenia-like psychoses after brain trauma. *Acta psychiat. et neurol. Suppl.* 60:36, 1951.
- ⁸⁸ Himler, Leonard E.: Psychiatric aspects of aging. *J.A.M.A.* 147:1330, 1951.
- ⁸⁹ Himwich, Harold E.: Thought processes as related to brain metabolism in certain abnormal conditions. *J. Nerv. & Ment. Dis.* 114:450, 1951.
- ⁹⁰ —: *Brain Metabolism and Cerebral Disorders*. Baltimore, Williams & Wilkins Co., 1951.
- ⁹¹ Historical notes: The word "psychiatry." *Am. J. Psychiat.* 107:628, 1951.
- ⁹² Historical notes: The word "psychiatry." *Am. J. Psychiat.* 107:868, 1951.
- ⁹³ Hoagland, Hudson: Some biochemical considerations of psychotic behavior. *J. Clin. & Exper. Psychopath.* 12:111, 1951.
- ⁹⁴ Hoch, Paul H.: Experimentally produced psychoses. *Am. J. Psychiat.* 107:607, 1951.
- ⁹⁵ Hope, Justin M.: Intravenous pervitin and the psychopathology of schizophrenia. *Dis. Nerv. System* 12:67, 1951.
- ⁹⁶ Hyroop, M.: Factor omnipotence in the development of paranoid reactions. *Am. J. Psychotherapy* 5:38, 1951.
- ⁹⁷ Jacobson, Avrohm: Brief psychotherapy of the war neuroses. Symposium on Military Medicine in the Far East Command, a Suppl. issue: The Surgeon's circular letter, Medical Section 123, Sept. 1951.
- ⁹⁸ Johnston, McClain: An experiment in group psychotherapy with the narcotic addict. *Am. J. Psychotherapy* 5:24, 1951.
- ⁹⁹ Kahn, Robert L. and Schlesinger, Benno: Preoperative and postoperative personality changes accompanying frontal lobe meningioma. *J. Nerv. & Ment. Dis.* 114:492, 1951.
- ¹⁰⁰ Kaldeck, Rudolph: Group psychotherapy by nurses and attendants. *Dis. Nerv. System* 12:138, 1951.
- ¹⁰¹ Kallmann, F. J.: Comparative twin data on the genetic aspects of mental disorders in the involutional and senile periods of life. *J. Gerontol.* 6:110, 1951.
- ¹⁰² Kamm, Bernard A.: Depressive, aggressive and paranoid reactions. *Psychoanalyt. Rev.* 38:127, 1951.
- ¹⁰³ Kaplan, Oscar J.: Place of psychology in gerontology. *Geriatrics* 6:298, 1951.
- ¹⁰⁴ Katz, Julius: Tuberculosis control in mental institutions. *N. Y. State J. Med.* 51:349, 1951.
- ¹⁰⁵ Kino, F. F.: Aliens' paranoid reaction. *J. Ment. Sc.* 97:589, 1951.
- ¹⁰⁶ Kioerboe, Erik: Suicide and attempted suicide among old people. *J. Gerontol.* 6:233, 1951.
- ¹⁰⁷ Kirk, John Esben: Steroid hormones and aging: a review. *J. Gerontol.* 6:253, 1951.
- ¹⁰⁸ Klein, J. J.: Study of unstable personalities after combat. *J. Nerv. & Ment. Dis.* 113:437, 1951.

- ¹⁰⁹ Klemes, M. A.: Therapeutic effect of group morale on a psychiatric hospital ward. *Bull. Menninger Clin.* 15:58, 1951.
- ¹¹⁰ Klineberg, Otto: National characteristics and international relations. *Am. J. Psychiat.* 107:661, 1951.
- ¹¹¹ Knight, Robert G. and Prout, Curtis T.: Study of results in hospital treatment of drug addictions. *Am. J. Psychiat.* 108:303, 1951.
- ¹¹² Kohl, Richard N.: Administrative aspects of a teaching hospital. *Am. J. Psychiat.* 107:481, 1951.
- ¹¹³ Kolansky, Harold and Cole, Richard K.: Field hospital neuropsychiatric service. Symposium on Military Medicine in the Far East Command, Suppl. issue: Surgeon's circular letter, Medical Section, 115, Sept. 1951.
- ¹¹⁴ Kornetsky, Conan H.: Psychological effects of chronic barbiturate intoxication. *Arch. Neurol. & Psychiat.* 65:557, 1951.
- ¹¹⁵ Kral, V. A.: Psychiatric observations under severe chronic stress. *Am. J. Psychiat.* 108:185, 1951.
- ¹¹⁶ Krapf, E. Eduardo: Sur la depersonnalisation. *Encephale.* 40:217, 1951.
- ¹¹⁷ Langfeldt, Gabriel: Diagnosis of schizophrenia. *Am. J. Psychiat.* 108:123, 1951.
- ¹¹⁸ Lasswell, Harold D.: Scientific study of bipolar attitudes. *Am. J. Psychiat.* 107:644, 1951.
- ¹¹⁹ Lehmann, H. E. and Kral, V. A.: Studies on the iron content of cerebrospinal fluid in different psychotic conditions. *Arch. Neurol. & Psychiat.* 65:326, 1951.
- ¹²⁰ Lemkau, Paul V.: Correspondence or letter to editor: mental health programs of the states. *Am. J. Psychiat.* 107:788, 1951.
- ¹²¹ —: Future organization of psychiatric care. *Psychiatric Quart.* 25:201, 1951.
- ¹²² Levin, Max: Delirium: a gap in psychiatric teaching. *Am. J. Psychiat.* 107:689, 1951.
- ¹²³ —: Clinical notes: experimental bromide intoxication; a criticism. *Am. J. Psychiat.* 108:309, 1951.
- ¹²⁴ Levin, Sidney: Psychomotor epilepsy as a manifestation of subdural hematoma. *Am. J. Psychiat.* 107:501, 1951.
- ¹²⁵ Lingjaerde, Ottar: Studies in schizophrenia. *Acta psychiat. et neurol.* 60:121, 1951.
- ¹²⁶ Lippman, Caro W.: Hallucinations in migraine. *Am. J. Psychiat.* 107:856, 1951.
- ¹²⁷ Liu, Chan-Nao: Cytology of rabbit neurons after "malononitrile" administration. *Arch. Neurol. & Psychiat.* 66:427, 1951.
- ¹²⁸ Luce, R. A. and Rothschild, D.: Correlation of electroencephalographic and clinical findings in psychiatric patients over 65. *J. Gerontol.* 6:121, 1951.
- ¹²⁹ Malamud, William, Hope, Justin M., and Elmadjian, Fred: Objective evaluation of therapeutic procedures in mental diseases. *Boston Med. Quart.* 2:1, 1951.
- ¹³⁰ Malmo, Robert B., Shagass, Charles, and Davis, John F.: Electromyographic studies of muscular tension in psychiatric patients under stress. *J. Clin. & Exper. Psychopath.* 12:45, 1951.
- ¹³¹ Mariner, Allen S.: Outpatient psychiatry in an overseas theater. Symposium on Military Medicine in the Far East Command, a Suppl. Issue: The surgeon's circular letter, Medical Section, 125, Sept. 1951.
- ¹³² Maslow, A. H. and Mittelmann, Béla: Principles of Abnormal Psychology: The dynamics of psychic illness. New York. Harper & Brothers, 1951.
- ¹³³ Mayer-Gross, W.: Experimental psychoses and other mental abnormalities produced by drugs. *Brit. M. J.* 2:317, 1951.

- ¹³⁴ McKinney, David W.: Problems of the self in the light of the psychopathology of schizophrenia. *Psychiatry*. 14:331, 1951.
- ¹³⁵ Meerloo, Joost A. M.: Crime of menticide. *Am. J. Psychiat.* 107:594, 1951.
- ¹³⁶ —: First aid in acute panic states. *Am. J. Psychotherapy*. 5:367, 1951.
- ¹³⁷ Menninger, Karl: Prescribing a therapeutic program. *Bull. Menn. Clinic* 15:167, 1951. Also Chapter V in *A Manual for Psychiatric Case Study*, New York, Grune & Stratton, 1952.
- ¹³⁸ Mental Hospitals, 1950. Proceedings of 2nd mental hospital institute held under auspices of Mental Hospital Service of American Psychiatric Association, St. Louis, Mo., Oct. 16-19, 1950. *Am. Psychiat. A.* 17:214, 1951.
- ¹³⁹ Merrell, David J.: Inheritance of manic-depressive psychosis. *Arch. Neurol. & Psychiat.* 66:272, 1951.
- ¹⁴⁰ Meyer, Adolf: Collected papers of Adolf Meyer. Vol. I. Neurology. Baltimore, Johns Hopkins Press, 1950.
- ¹⁴¹ —: Collected papers of Adolf Meyer. Vol. II. Psychiatry. Baltimore, Johns Hopkins Press, 1951.
- ¹⁴² —: Collected papers of Adolf Meyer. Vol. III. Medical Teaching. Baltimore, Johns Hopkins Press, 1951.
- ¹⁴³ Moore, Robert A.: Orientation of the problems of aging. *J.A.M.A.* 147:1327, 1951.
- ^{143a} Moore, T. V.: *Nature and Treatment of Mental Disorders*. New York, Grune & Stratton, 1951.
- ¹⁴⁴ Moriarty, John D.: Nutrition applied to clinical psychiatry. *Dis. Nerv. Sys.* 12:105, 1951.
- ¹⁴⁵ Morris, Charles: Clinical notes: similarity of constitutional factors in psychotic behavior in India, China and the United States. *Am. J. Psychiat.* 108:143, 1951.
- ¹⁴⁶ Muncie, Wendell and Billings, Edward G.: Survey of conditions of private psychiatric practice throughout the United States and Canada. *Am. J. Psychiat.* 108:171, 1951.
- ¹⁴⁷ Murphy, B. W.: Some interpersonal processes and situations delaying discharge from a psychiatric institute. *Dis. Nerv. System*. 12:273, 1951.
- ¹⁴⁸ Noack, C. H. and Trautner, E. M.: Lithium treatment of maniacal psychosis. *M. J. Australia*. 2:219, 1951.
- ¹⁴⁹ Noble, Douglas: Hysterical manifestations in schizophrenic illness. *Psychiatry*, 14:153, 1951.
- ¹⁵⁰ —: Study of dreams in schizophrenia and allied states. *Am. J. Psychiat.* 107:612, 1951.
- ¹⁵¹ Oltman, Jane E. and Friedman, Samuel: Electrocardiogram in psychiatric patients. *J. Nerv. & Ment. Dis.* 113:127, 1951.
- ¹⁵² Palmer, G. Blake: Some drug-induced and other toxic psychoses. *New Zealand M. J.* 50:292, 1951.
- ¹⁵³ Papez, James W. and Bateman, J. F.: Changes in nervous tissues and study of living organisms in metal disease. *J. Nerv. & Ment. Dis.* 114:400, 1951.
- ¹⁵⁴ Pasquarelli, Blaise: Experimental investigation of the body-mind continuum in affective states. *J. Nerv. & Ment. Dis.* 113:512, 1951.
- ¹⁵⁵ Pearson, G. B. and Ferguson, J.O.: Nuns' melancholy. *Dis. Nerv. System* 12:295, 1951.
- ¹⁵⁶ Pomerat, C. M.: Pulsatile activity of cells from the human brain in tissue culture. *J. Nerv. & Ment. Dis.* 114:430, 1951.
- ¹⁵⁷ Prados, Miguel: Use of films in psychiatry. *Orthopsychiatry* 21:36, 1951.
- ¹⁵⁸ Pratt, R. T. C.: An investigation of the psychiatric aspects of disseminated sclerosis. *J. Neurol., Neurosurg. & Psychiat.* 14:326, 1951.

- ¹⁵⁹ Rado, Sandoz: Psychodynamics of depression from the etiologic point of view. *Psychosom. Med.* 13:51, 1951.
- ¹⁶⁰ Raevuori-Nallinmaa, Sole: Brain injuries attributable to boxing. *Acta Psychiat. et neurol.* 60:51, 1951.
- ¹⁶¹ Randall, Ollie A.: Sociological aspects of aging. *J.A.M.A.* 147:1325, 1951.
- ¹⁶² Rees, Linford and King, G. M.: Desoxycortone acetate and ascorbic acid in the treatment of schizophrenia. *J. Ment. Sc.* 97:376, 1951.
- ¹⁶³ Reid, John R. and Finesinger, Jacob E.: Inference testing in psychotherapy. *Am. J. Psychiat.* 107:894, 1951.
- ¹⁶⁴ Reiss, M., Hemphill, R. E., Maggs, R., Smith, S., and Reiss, Jean M. Thyroid activity in mental patients. *Brit. M. J.* 1:1181, 1951.
- ¹⁶⁵ Ripley, Herbert S. and Wolf, Stewart: Studies in psychopathology. *J. Nerv. & Ment. Dis.* 114:234, 1951.
- ¹⁶⁶ —: Long-term study of combat area schizophrenic reactions. *Am. J. Psychiat.* 108:409, 1951.
- ¹⁶⁷ Ritchie, John A.: Adrenergic and cholinergic properties of blood. *J. Nerv. & Men. Dis.* 114:307, 1951.
- ¹⁶⁸ Robinson, G. W., Jr.: Severe functional mental disease in extreme old age. *J. Geron-tol.* 6:141, 1951.
- ¹⁶⁹ Roger, H. and Poursines, Y.: Formes psychosiques des meningo-neurobrucelloses. *Ann. med.-psychol.* 109:145, 1950.
- ¹⁷⁰ Rud, Finn: Social psychopathology of the schizophrenic states. *J. Clin. & Exper. Psychopath.* 12:67, 1951.
- ¹⁷¹ Ruesch, Jurgen and Bateson, Gregory: Communication, The Social Matrix of Psychiatry. New York, W. W. Norton & Co. Inc., 1951.
- ¹⁷² Rusk, Howard: Geriatrics and rehabilitation. *Geriatrics.* 6:143, 1951.
- ¹⁷³ Russell, William L.: Letter to the editor: mental health programs of the states. *Am. J. Psychiat.* 107:709, 1951.
- ¹⁷⁴ Sackler, Arthur M., Sackler, Mortimer D., Sackler, Raymond R., Tui, Co, and van Ophuijsen, Johan H. W.: On the pathogenesis of certain psychiatric disorders. Part V. Endocrinologic orientation to psychiatric disorders. *J. Clin. & Exper. Psychopath.* 12:30, 1951.
- ¹⁷⁵ —: An appraisal of the current status of sex steroid biochemotherapy in psychiatry. Part III. Endocrinologic orientation to psychiatric disorders. *J. Clin. & Exper. Psychopath.* 12:15, 1951.
- ¹⁷⁶ —: An appraisal of the current status of histamine biochemotherapy in psychiatry and the theoretical significance of its effects. Part II. Endocrinologic orientation to psychiatric disorders. *J. Clin. & Exper. Psychopath.* 12:5, 1951.
- ¹⁷⁷ St. Clair, Harvey R.: Psychiatric interview experiences with negroes. *Am. J. Psychiat.* 108:113, 1951.
- ¹⁷⁸ Scheffen, Albert E.: Malignant tumors in the institutionalized psychotic population. *Arch. Neuro. & Psychiat.* 66:145, 1951.
- ¹⁷⁹ Scheid, Phil N.: Training the overage employee for retirement. *J.A.M.A.* 147:1323, 1951.
- ¹⁸⁰ Schlesinger, Benno: Gliomas involving the splenium of the corpus callosum. *New York Neurol.* 1:419, 1951.
- ¹⁸¹ Schmideberg, Walter: Agoraphobia as a manifestation of schizophrenia: analysis of a case. *Psychoanalyt. Rev.* 38:343, 1951.
- ¹⁸² Schwab, Robert S., Fabing, Howard D., and Prichard, John S.: Psychiatric symptoms and syndromes in Parkinson's disease. *Am. J. Psychiat.* 107:901, 1951.

- ¹⁸³ Schwartz, Charlotte Green, Schwartz, Morris S., and Stanton, Alfred H.: Study of need-fulfillment on a mental hospital ward. *Psychiatry*. 14:223, 1951.
- ¹⁸⁴ Sechehayé, M. A.: Symbolic Realization; A new method of psychotherapy applied to a case of schizophrenia. New York, International Universities Press, Inc., 1951.
- ¹⁸⁵ —: Autobiography of a Schizophrenic Girl, With Analytic Interpretation (translated by Grace Rubin-Rabson). New York, Grune & Stratton, 1951.
- ¹⁸⁶ Seitz, Philip F. Durham: A dynamic factor correlated with the prognosis in paranoid schizophrenia. *Arch. Neurol. & Psychiat.* 65:604, 1951.
- ¹⁸⁷ Sewall, Lee G. and Grady, Charles W.: Utilizing the community as a therapeutic resource. *Am. J. Psychiat.* 108:456, 1951.
- ¹⁸⁸ Sheffel, Irving: Administration; a point-of-view for psychiatrists. *Bull. Menninger Clin.* 15:131, 1951.
- ¹⁸⁹ Shock, N. W.: Trends in Gerontology. Stanford, California, Stanford University Press, 1951.
- ¹⁹⁰ —: Classified Bibliography of Gerontology and Geriatrics. Stanford, California, Stanford University Press, 1951.
- ¹⁹¹ Siegal, Lewis J.: Amnesia—its integrative analysis in psychopathological orientation. *Arch. Neuro. & Psychiat.* 66:700, 1951.
- ¹⁹² Siegel, Miriam G., Sackler, Mortimer D., Sackler, Arthur M., Sackler, Raymond R., and van Ophuijsen, Johan H. W.: Improvement in schizophrenics following histamine and steroid therapy as revealed in psychological tests. Part IV. Endocrinologic orientation to psychiatric disorders. *J. Clin. & Exper. Psychopath.* 12:25, 1951.
- ¹⁹³ Simon, Alexander: Psychological problems of aging. *California Med.* 75:73, 1951.
- ¹⁹⁴ Simon, Benjamin, Holzberg, Jules D., Alessi, Salvatore L., and Garrity, Daniel A.: Recognition and acceptance of mood in music by psychotic patients. *J. Nerv. & Ment. Dis.* 114:66, 1951.
- ¹⁹⁵ Simon, Werner and Garvey, James T.: Glucose tolerance in chronic schizophrenia and senile states. *Arch. Neurol. & Psychiat.* 65:717, 1951.
- ¹⁹⁶ Simpson, William S.: Chronic psychosis as a sequel to measles encephalitis. *Bull. Menninger Clin.* 15:141, 1951.
- ¹⁹⁷ Solomon, Harry C.: Treatment of the psychoses. *Psychiatric Quart.* 25:1, 1951.
- ¹⁹⁸ Soniat, T. L. L.: Psychiatric symptoms associated with intracranial neoplasms. *Am. J. Psychiat.* 108:19, 1951.
- ¹⁹⁹ Spiegel, E. A., Wycis, H. T., Freed, H., and Orchinik, C.: Central mechanism of the emotions. *Am. J. Psychiat.* 108:426, 1951.
- ²⁰⁰ Stein, Marvin, Ronzoni, Ethel, and Gildea, Edwin F.: Physiological responses to heat stress and ACTH of normal and schizophrenic subjects. *Am. J. Psychiat.* 108:450, 1951.
- ²⁰¹ Stern, Karl, Williams, Gwendolyn M., and Prados, Niguel: Grief reactions in later life. *Am. J. Psychiat.* 108:289, 1951.
- ²⁰² Stevenson, G. H.: Prevention of recurring manic-depressive illnesses. *Canad. M.A.J.* 64:198, 1951.
- ²⁰³ — and Geoghegan, J. J.: Prophylactic electroshock; a five-year study. *Am. J. Psychiat.* 107:743, 1951.
- ²⁰⁴ Stokes, W. R.: Sexual function in aging male. *Geriatrics.* 6:304, 1951.
- ²⁰⁵ Strecker, Edward A., Ebaugh, Franklin G., and Ewalt, Jack R.: Practical clinical psychiatry. New York, Blakiston Co., 1951.
- ²⁰⁶ Stycos, J. Mayone: Family care. *Psychiatry.* 14:301, 1951.

- ²⁰⁷ Swartz, Jacob and Semrad, Elvin V.: Psychosomatic disorders in psychoses. *Psychosom. Med.* 13:314, 1951.
- ²⁰⁸ Szalita-Pemow, Alberta: Remarks on pathogenesis and treatment of schizophrenia. *Psychiatry* 14:295, 1951.
- ²⁰⁹ Tait, C. Downing, Jr. and Burns, G. C.: Involutional illnesses; survey of 379 patients, including follow-up study of 114. *Am. J. Psychiat.* 108:27, 1951.
- ²¹⁰ Teuber, Hans-Lukas, Battersby, William S., and Bender, Morris B.: Performance of complex visual tasks after cerebral lesions. *J. Nerv. & Ment. Dis.* 114:413, 1951.
- ²¹¹ Tolsma, F. L.: Modern psychiatric views on the induced psychosis. *Folia psychiat. neurol. et neurochir. neerl.* 54:300, 1951.
- ²¹² Tompkins, H. J.: Aged patient in the public psychiatric hospital. *Geriatrics.* 6:57, 1951.
- ²¹³ Tui, Co: Somatologic perspectives in psychiatric research. Part VI. Endocrinologic orientation to psychiatric disorders. *J. Clin. & Exper. Psychopath.* 12:35, 1951.
- ²¹⁴ Tyhurst, J. S.: Individual reactions to community disaster; natural history of psychiatric phenomena. *Am. J. Psychiat.* 107:764, 1951.
- ²¹⁵ Tyhurst, Libuse: Displacement and migration, a study of social psychiatry. *Am. J. Psychiat.* 107:561, 1951.
- ²¹⁶ Usdin, Gene L. and Robinson, Kent E.: Psychosis occurring during antabuse administration. *Arch. Neurol. & Psychiat.* 66:38, 1951.
- ²¹⁷ Vanderveldt, Rev. James: Religion and mental health. *Ment. Hyg.* 35:177, 1951.
- ²¹⁸ van Ophuijsen, J. H. W.: Endocrinologic orientation to psychiatric disorders. Part I and introduction: A new phase in clinical psychiatry. *J. Clin. & Exper. Psychopath.* 12:1, 1951.
- ²¹⁹ Waelder, Robert: Structure of paranoid ideas; a critical survey of various theories. *Internat. J. Psycho-Analysis.* 32:167, 1951.
- ²²⁰ Wassersug, J. D., and McLaughlin, W. F.: Tuberculosis in mental hospitals. *J. Nerv. & Ment. Dis.* 113:115, 1951.
- ²²¹ Wexler, Milton: Structural problem in schizophrenia; the role of the internal object. *Bull. Menninger Clin.* 15:221, 1951.
- ²²² Whitehorn, John C.: Presidential address; individual psychiatrist and social psychiatry. *Am. J. Psychiat.* 108:1, 1951.
- ²²³ Wikler, Abraham: Clinical aspects of diagnosis and treatment of addictions. *Bull. Menninger Clin.* 15:157, 1951.
- ²²⁴ Williams, E. Y.: Treatment of drug addiction. *Psychiatric Quart.* 25:604, 1951.
- ²²⁵ Wittenborn, J. R. and Lesser, Gerald S.: Biographical factors and psychiatric symptoms. *J. Clin. Psychol.* 7:317, 1951.
- ²²⁶ Wittson, Cecil L. and Hunt, William A.: Predictive value of the brief psychiatric interview. *Am. J. Psychiat.* 107:582, 1951.
- ²²⁷ Worden, Frederic G.: Psychotherapeutic aspects of authority. *Psychiatry.* 14:9, 1951.
- ²²⁸ Yap, P.-M.: Mental diseases peculiar to certain cultures; a survey of comparative psychiatry. *J. Ment. Sc.* 97:313, 1951.
- ²²⁹ Yerbury, Edgar C., Holzberg, Jules D., and Alessi, Salvatore L.: Psychological tests in the selection and placement of psychiatric aides. *Am. J. Psychiat.* 108:91, 1951.
- ²³⁰ Zimmering, Paul, Toolan, James, Safrin, Renate, and Wortis, S. Bernard: Heroin addiction in adolescent boys. *J. Nerv. & Ment. Dis.* 114:19, 1951.

Genetics in Neurology and Psychiatry

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DURING the past decades research on human genetics has, with constant reference to experimental genetics, mathematical statistics, and clinical research, made considerable advances. With the help of so-called *family-research*, diseases were analyzed, usually, rare ones, in which simple Mendelian laws of heredity could be demonstrated, as for instance in cases of myoclonus epilepsy, juvenile amaurotic idiocy, Huntington's chorea, etc.

Important discoveries in the field of experimental genetics have shown, however, that a monohybrid main gene need by no means always be manifested in the classical Mendelian ratios. We must thus reckon with *penetrance*, *expressivity*, *sex-controlled inheritance*, *partial sex-linkage* and *multifactorial inheritance*. An excellent account of these matters has been given by Fraser Roberts.²³

Another important branch of psychiatric genetics is concerned with *population studies*. Population studies are of great importance, from both the theoretic and the practical point of view. They afford possibilities of establishing the frequency of mental disorders in an average population and of studying the age of onset and the mortality of the various diseases. They also make possible calculations of the morbidity risks and assessment of the need for institutional care, etc. If they are combined with investigations of the pedigree, it is also possible to study the risks of disease for various categories of relatives of the diseased persons and thus to obtain a basis for judging the hereditary risks. Population studies also give good opportunities for an analysis of the significance of various environmental factors (different countries, isolated groups, rural population versus urban population, different religious and social strata, etc.).

That such investigations, performed with exact methods, should be carried out in different countries is an urgent desideratum.

Research on twins has always been an important branch of genetic research. The method involves, however, several sources of error which are difficult to control and which call for careful attention. These include various prenatal, natal, and postnatal factors. Critical studies of the present position of research on twins and different biases in twin studies have been made particularly by v. Verschuer²⁴ and Price.²²

There is a paucity of textbooks and accounts summarizing the methods of research used in human genetics. Fraser Roberts' standard work is now somewhat out-of-date in several respects, but a new edition is expected. Recently, a valuable introduction to human genetics has been published by Kemp.¹⁵

A textbook of human genetics by Stern³⁰ has many stimulating references to experimental genetics. It gives a good account of human genetics, though one sometimes notices that the writer is not a specialist in this latter field. To be recommended highly is Penrose's²¹ recently published excellent survey.

GENETIC PSYCHIATRIC POPULATION STUDIES

A clear, critical and relatively comprehensive survey of this subject is given by Strömgren,³¹ whose important work published in 1938 entitles him to be regarded as one of the founders of the modern type of psychiatric population study.

Sjögren²⁵ has published a psychiatric study of a Swedish rural population. The total number of genealogically studied persons was about 9000. The investigation covers the period from 1900-1944 and is based upon a study of all the hospitals where sick persons from this area were admitted for treatment and also upon extensive field studies. The frequency of marriage between cousins in the average population in this area was 3 per cent, a figure that may be considered significant for an average Swedish rural population (cf. Böök⁴). The morbidity-risk was determined for a large number of mental diseases, both for the average population and for the siblings of the sick *propositi*.^{*} Sjögren's morbidity-risk figures show good agreement with those arrived at in earlier investigations. Frequency-figures for presenile and senile psychoses in the population previously had not been published. After correction for the increased mortality, the figure was as high as 1.1 per cent. The corresponding figure for schizophrenia, manic-depressive psychosis and the more severe cases of oligophrenia (idiocy and severe imbecility) was about 1 per cent.

The first genetic-statistical population study from Norway recently was published by Bremer.⁸ The writer has, for several years, practiced as a doctor in the district with which he deals, and he thus has a thorough

^{*} Since non-geneticists may not be familiar with some of the technical terms used in this chapter it may be advisable to give their definition. *Proband* and *propositus* are defined in Dorland's American Medical Dictionary as the original person presenting a mental or physical disorder who serves as the basis for a genetic study. *Expressivity* is defined in Gould's Medical Dictionary as the degree to which a given gene manifests itself in the hereditary characteristic which it governs. *Penetrance* is defined in Gould's Medical Dictionary as the percentage of organisms having a given genetic constitution which show the corresponding hereditary character.

personal knowledge of the people and of their environment. He has, therefore, been able to record the milder forms of mental disorders also, such as neuroses, psychopathies and less severe cases of oligophrenia. Among 1000 persons of over ten years of age, the author found the following frequencies of mental diseases: psychoses 3.6 per cent, neuroses and psychopathies 14.9 per cent, and oligophrenias together 5.6 per cent. It must, however, be pointed out that the population in question is that of an isolated fishing village with, in several respects, special conditions. The morbidity-risks for psychoses do, nevertheless, show good agreement with those found in earlier population studies.

It is interesting to compare Bremer's figures concerning psychopathy and neuroses with those found by a Swedish investigator, Ekblad.¹⁰ This writer examined a representative group of 310 naval conscripts, and found an incidence of approximately 15 per cent. This figure agrees rather well with Bremer's, which is 12 per cent for men.

In a preliminary report, Mayer-Gross¹⁸ gives an account of an important mental health survey in a rural area in Scotland. The district in question has 56,000 inhabitants. The author has collaborated with a number of authorities and institutions. Only a limited number of cases, however, had been seen by psychiatrists. All the children under the age of 11 years were subjected to intelligence tests. 5105 persons, i.e., 9 per cent of the total population, were found to be abnormal. The "dull and backward," who had an I.Q. between 70 and 80, comprised 2.85 per cent of the population, and the mental defectives comprised 1.65 per cent. There were 1.9 per cent neurotics and psychopaths, 0.35 per cent suffering from affective psychoses, 0.42 per cent with schizophrenia, 0.6 per cent with senile or arteriosclerotic psychoses, 0.17 per cent were epileptics and 0.39 per cent alcoholics.

A study of an isolated population in northernmost Sweden comprising 9000 persons has been reported in a preliminary report by Böök.⁵ It is interesting to note that his analysis of the morbidity-risk for schizophrenia gave the high figure of 2.85 ± 0.30 per cent.

FAMILY INVESTIGATIONS

Thomassen³² makes a thorough clinical and genealogic investigation on material collected from 29 living patients suffering from Thomsen's disease and 101 living patients with dystrophia myotonica. He analyzes these diseases with reference to the geographic distribution in Denmark; distributions according to the patients' sex, age, life expectancy, the age of manifestations, fertility in the families and mortality. He finds increased child-mortality in cases of dystrophia myotonica. He did not notice any evidence that Thomsen's disease and dystrophia myotonica are genetically identical. In the majority of cases, the author finds that the heredity in Thomsen's

disease is dominant. A very large pedigree shows direct dominant inheritance in seven generations. The genetic-statistical analysis of dystrophia myotonica clearly indicates monohybrid, autosomal, dominant heredity. It should, however, be pointed out that the author assumes that cases of isolated cataract are monosymptomatic cases of dystrophia myotonica.

Brandt⁷ has published a valuable work on infantile progressive muscular atrophy (Werdnig-Hoffmann). He has collected a large amount of material of 156 cases, including 131 primary cases. The patients are equally distributed between the sexes. With Weinberg's proband method the author finds a Mendelian figure of 30 per cent and an inbreeding rate of 4.2 per cent of marriage between cousins. He suggests that, for certain families, a dominant inheritance with reduced penetrance is probable. For the majority of cases he considers a recessive heredity as most probable. It is difficult, however, to draw any definite conclusions in this last-mentioned respect on the strength of the author's material.

Borberg⁶ has collected and analyzed, from clinical and genetic points of view, numerous cases of tuberous sclerosis and Recklinghausen's neurofibromatosis. The propositi with tuberous sclerosis, a total of 37, were divided clinically into 26 severe cases and 11 abortive cases. The propositi suffering from Recklinghausen's neurofibromatosis numbered 84. The hereditary conditions were investigated on the basis of data concerning 35 families with tuberous sclerosis and 79 families with Recklinghausen's neurofibromatosis. The author arrives at the well-founded conclusion, that both these diseases are independent from the genetic point of view. The genetic analysis indicates a monohybrid, autosomal, dominant inheritance with a great variability of manifestation for both diseases. In six families with tuberous sclerosis the author finds unquestionable inheritance covering 2 or 3 generations, in four other families likely inheritance, and in another four families doubtful inheritance. In the remaining 21 families no signs of inheritance were observed. The author assumes that this is due chiefly to new mutations. The solitary cases can, however, also be explained by the fact that the author has missed a number of secondary cases. This would appear probable, partly because the penetrance has been shown to be reduced, and partly because the expressivity of the disease is variable right down to micro-forms, and is, therefore, difficult to diagnose. Finally, it cannot be considered as entirely out of the question that the disease may, in certain cases, follow a recessive pattern of inheritance. As regards Recklinghausen's neurofibromatosis, unquestionable direct inheritance has been demonstrated in at least two generations in 30 out of 79 families, while in the other families it has not been possible to show any inheritance. The author's genetic argument is conducted in the same way as in connection with tuberous sclerosis.

Levison¹⁷ deals with a large and representative material of progressive muscular dystrophy comprising 110 *propositi* classified in 3 different groups: (1) the scapulohumeral type (Erb); (2) the facioscapulohumeral type (Landouzy-Déjérine); (3) the lower extremity type. He subjects his material to a detailed genetic-statistical analysis. It appears that in the typical facioscapulohumeral type inheritance is dominant in most cases. The scapulohumeral and the intermediate types between the scapulohumeral and the facioscapulohumeral types are all, except one, sporadic cases. The pedigrees belonging to four families in the lower extremity group indicate that the disease is inherited through healthy females by the sons; it may be sex-linked or sex-limited, recessive. The genetic-statistical analysis of the other families in group 3 gives considerably lower Mendelian figures (13-15 per cent) than are theoretically to be expected in connection with a monohybrid recessive heredity. The author, therefore, suggests reduced manifestation and an admixture of non-genetic cases. One fact, however, does not agree with the assumption of a monohybrid recessive heredity. The frequency of consanguineous marriages is not increased in the parents of those *propositi*.

Sjögren and Larsson²⁷ have published a monograph on microphthalmus and anophthalmus with or without coincident oligophrenia. Their investigation is based upon a large and representative material that has been collected from the schools for the blind in different parts of the country in the course of the past 50 years. This comprises 137 cases of microphthalmus or anophthalmus, 58 of which have been combined with oligophrenia. A combination with other malformations was common: cataract, coloboma and skeletal anomalies. Toxoplasmosis, lues and rubeola in the mother during the pregnancy can only explain a few of the cases. The genetic analysis shows a recessive sex-linked inheritance for certain families. The possibility of a partial sex-linked inheritance with reduced manifestation is discussed. The authors point out that the possibility of separate forms of inheritance cannot be ruled out, so that the families in the pedigree charts may thus, for example, follow a totally sex-linked recessive mode; otherwise, it may be a matter of both a partially sex-linked recessive mode of inheritance and mutations with a dominant appearance. It has not been possible to determine the extent to which cases caused by non-genetic factors occur among the isolated cases of microphthalmus combined with oligophrenia.

Sjögren²⁶ has also published an investigation of hereditary congenital spinocerebellar ataxia accompanied by congenital cataract and oligophrenia. The disease has previously been described only once, by Marinesco, Draganesco and Vasiliu 1931. These writers, however, did not carry out any genetic-statistical analysis of the disease. We have an extremely rare

mutation here. Sjögren's material comprises 14 cases belonging to six families. The genetic-statistical analysis shows a recessive, monohybrid, autosomal mode of inheritance.

Mjones¹⁹ has published a valuable clinical and genetic monograph on paralysis agitans. This study is based upon a personally examined and genealogically investigated material of 250 cases of paralysis agitans. The author groups the 250 *propositi* in the following way: paralysis agitans (194 cases), arteriosclerotic parkinsonism (32 cases) and parkinsonism (24 cases). Among the relatives of 79 of the 194 *propositi* suffering from paralysis agitans, the author has found 162 secondary cases.

The investigation gives no support to the view that paralysis agitans *juvenilis* is an independent form of disease. Considerable intrafamilial variation is found, and micro-forms, e.g., isolated tremor, are not uncommon. From the genetic-statistical analysis it emerges that the heredity for cases of paralysis agitans belonging to groups 1 and 2 (families with secondary cases and parent-mating healthy $\times$ affected and healthy $\times$ healthy) is with a high degree of probability monohybrid, autosomal, dominant. A determination of the Mendelian ratio gives about 30 per cent. The author thinks it probable that in the families collected in group 2 the loss of secondary cases is especially marked. The parent-mating healthy $\times$ healthy is thus apparent in at least the majority of cases, and the two groups doubtless represent the same nosologic entity. The author considers that an inhibition of manifestation constitutes the chief reason why the expected Mendelian ratio of 50 per cent is not attained. The degree of manifestation is estimated as about 60 per cent. Group 3, containing solitary cases, probably consists of both genetically and non-genetically conditioned cases. It is not possible clinically to distinguish these from one another. The only valid criterion for the diagnosis hereditary paralysis agitans is the demonstration of secondary cases.

On the subject of specific dyslexia (congenital word-blindness) we have a clinical and genetic monograph by Hallgren.¹¹ This work is based upon a personally examined representative material of 273 cases of specific dyslexia, including 117 *propositi*. With the help of statistical methods, the author analyses the importance of different possible environmental factors for the origin of specific dyslexia. He finds in any case for the main groups, comprising about 80 per cent of the material, no evidence that such factors have any causal significance. On the other hand, the genetic-statistical analysis shows that in these groups specific dyslexia follows a monohybrid, autosomal, dominant heredity with practically complete manifestation, at least among men. There is possibly a reduced manifestation among women. In the overwhelming majority of families, i.e., in 90 out of 112 (80 per cent), the parent-mating is affected $\times$ unaffected. The Mendelian ratios are cal-

culated with various methods. With Weinberg's proband method the ratio is 45.7 ± 4.3 per cent. The parent-mating unaffected $\times$ unaffected occurs in 19 families. The material in these families is presumably heterogeneous. It has not been possible to determine the extent to which secondary dyslexia occurs among the solitary cases.

Åmark² has published a valuable monograph on alcoholism in its clinical, social-psychiatric and genetic aspects. His primary material, consisting of 645 alcoholics, has been taken in part from the psychiatric clinic of Karolinska sjukhuset in Stockholm (103 cases), in part from 10 different institutions for alcoholics in Sweden (100 cases) and, finally, from the Temperance Board in Stockholm (441 cases). The author has calculated the morbidity-risk figures for psychoses and other abnormal psychic states in parents and siblings. Comparisons with the frequencies of schizophrenia, manic-depressive psychosis, general paresis, epilepsy and oligophrenia in the general population show no statistically significant differences. Among all the siblings and parents the frequency of psychopathy is about 15 per cent. A comparison with Fremming's frequency for the general population gives statistically well established differences. The morbidity-risk in respect to alcoholism for the brothers as well as the fathers is about 25 per cent. For men, in the general population in Denmark, Fremming obtained the frequency 3.41 ± 0.44 per cent.

The genetic analysis is based upon 203 propositi and 105 secondary cases. It shows that hereditary factors are of great significance in the origin of alcoholism, at least as regards certain types of alcoholism. The author has also made an interesting analysis of the frequency of psychopathy among the siblings of the primary cases. He finds the same frequency, about 15 per cent, among the siblings who grew up in good home conditions as among those who grew up in bad home conditions. On the other hand, he finds a significantly higher frequency of psychopathy in connection with the parent-mating healthy $\times$ psychopathic than with the parent-mating healthy $\times$ healthy, viz., 22.7 ± 2.7 per cent and 10.5 ± 1.4 per cent respectively.

There are remarkably few genetic studies on epilepsy. There are Conrad's important investigations of asylum material and the papers of Lennox, and of Lennox and Gibbs.

A comprehensive monograph on epilepsy in its clinical, social, and genetic aspects is published by Alström.¹ The material, which has been made the subject of thorough clinical and genealogic investigations, comprises 897 patients from the Neurological Clinic of the Caroline Institute in Stockholm and from the professor's private practice. The material may be said to be representative for cases of epilepsy treated in open wards; the epileptic clientèle of asylums, on the other hand, is not represented. The asylum

material, however, constitutes quantitatively only a fraction as compared with the milder cases of epilepsy. The author classifies his material in three groups with unknown (U), probable (P) and known (K) etiology. Sixty-eight per cent belong to the U group, the remainder being more or less equally divided between P and K. The author has made valuable studies on prognosis, mortality, and fertility. The percentage of patients affected mentally in the groups U, P and K is 21, 37 and 58 per cent respectively. The genetic-statistical analysis of the different groups gives the following results: In the whole series the frequency of epilepsy for parents is 1.3 ± 0.27 , for siblings 1.5 ± 0.25 and for children 3.0 ± 0.93 per cent. The groups U, P and K show slight, probably chance, deviations from these figures. The morbidity-risk figures for parents, siblings and children of the mentally affected *propositi* with epilepsy due to unknown causes are 1.4 ± 0.70 , 1.5 ± 0.61 and 2.7 ± 2.60 per cent respectively. The frequency of psychoses and severe forms of oligophrenia in the groups of relatives is in good agreement with the corresponding figures for the general rural population in Sweden found by Sjögren.

In about one per cent of the 897 *propositi*—11 *propositi* belonging to 8 families—the epileptic manifestation appears to be a symptom in a genetically determined monohybrid disease. The pattern of transmission is probably recessive in four, and dominant in seven, families. The author discusses different patterns of inheritance. He draws attention to the possibility of a dominant main gene and modifying polygenes determining the epileptic manifestations in general. He considers, however, that a more likely hypothesis is that epilepsy, even that in a so-called “nuclear group,” is not a disease *sui generis*, but is to be interpreted as an unspecific neurologic clinical symptom of a pathologic irritation of the central nervous system, focal in origin. The basic diseases may be hereditary—i.e., gene-determined, rare neuropsychiatric disorders—or, and most commonly, they may be diseases not determined by genes, but by injuries, infections, etc. According to our opinion, the author underestimates the significance of a multifactorial inheritance. Alström criticizes the work on epilepsy by Lennox and Gibbs. He goes too far but the criticism is justified inasmuch as it draws attention to the fact that electroencephalographic diagnosis is uncertain and that a large and representative control material must be examined before reliable conclusions can be drawn.

Lennox¹⁶ has published a summary of his investigations over a number of years of 4231 patients examined by himself and his colleagues. The author determines the number of affected persons among the patients, parents, siblings, and children (altogether 20,000 persons), obtaining, for the incidence of epilepsy, the figure 3.2 per cent. For the group with brain injury the incidence was 1.8 per cent. The author has also published much

material on twins and arrived at a result which, in respect to concordance, is in full agreement with that obtained by Conrad. He finds that concordance is usual, not only with regard to seizures, but also with regard to the type of seizure and to the EEG pattern. A detailed account of, *inter alia*, the way in which the material was collected, the representativity, the criteria of uniovularity, and the method with which the figures for the morbidity-risk are calculated must be given before it is possible to take up a definite position regarding the author's findings.

An interesting departure is to be found in the work on Huntington's chorea by Patterson, Bagchi, and Test.²⁰ The authors analyse the electroencephalographic findings in 26 offspring of parents with Huntington's chorea. Nineteen (73 per cent) of the subjects showed definite EEG abnormalities, particularly in the motor regions. Of those, 12 showed a high degree of EEG abnormality and the authors presume that these subjects may later manifest the disease. The remaining seven cases showed less pronounced EEG changes, and the authors suppose that there is a certain probability of their manifesting Huntington's chorea. The definite answer will depend upon follow-up observations in the future.

Bleuler⁸ and his school have, for several years, in a number of stimulating papers, published investigations dealing with the borderland between endocrinology and psychiatry. Of particular interest are their studies on schizophrenias and psychopathies appearing in acromegalic subjects. Family researches suggest a genetic causation, perhaps of a dominant character, in the families investigated. Also, other studies by this school on schizophrenia combined with other endocrine disturbances are of great interest. They aim at isolating from the great schizophrenic group possible clinical entities. An extension of these studies is desirable, in order to ensure further the reliability of the genetic-statistical analysis.

Schut²⁴ has published a large pedigree of hereditary ataxia. The 22 personally examined members of the family are divided clinically into four disease forms. Cases of Friedreich's ataxia, hereditary cerebellar ataxia, as well as hereditary spastic paraplegia are represented. Five of the cases have been examined histopathologically. In the family in question the disease obviously is dominant, but a genetic-statistical analysis of the Mendelian figures would have been desirable.

Stephens and Tyler²⁵ report a genetic study of the inheritance of childhood progressive muscular dystrophy in 33 families. The authors have material regarding 63 dystrophic individuals belonging to 33 separate families. The disease was manifest only in the males. In seven of the families studied the trait is clearly transmitted as a sex-linked recessive with the possible alternative of an autosomal trait occurring in the heterozygotic males but not in the heterozygotic females. In 14 families there were

insufficient data from which to draw definite conclusions as to the inheritance of the trait, and in 12 families there was definite evidence that if the trait is due to a sex-linked recessive gene the cases must represent new mutations. Sjövall's excellent clinical-genetic work from 1936 on a large and representative material of progressive muscular dystrophy has unfortunately been overlooked.

Hanhart¹² has published an interesting pedigree with 25 cases of progressive muscular dystrophy (Duchenne-Griesinger's type). The genetic-statistical analysis shows a recessive monohybrid inheritance is probable.

In a monograph on a muscular disease—"myopathia distalis tarda hereditaria"—Welander³⁴ deals with an illness previously not described. The investigation is based upon 249 examined cases in 72 pedigrees. The published pedigrees obviously indicate a monohybrid autosomal dominant inheritance. No more detailed genetic-statistical analysis has yet been published, however.

Denny-Brown⁹ has published a clinical, genetical, and histopathologic study of sensory radicular neuropathy. Hicks' pedigree from 1922 has been supplemented, and the author has found 11 affected individuals in three generations, which obviously indicates a monohybrid dominant inheritance.

RESEARCH ON TWINS

Kallmann has, in a number of papers, given an account of the results obtained from a very large population of twins. The most important results have been published in a preliminary report.¹⁴ The material comprises 1232 psychotic twin index cases. The value of the investigation is enhanced by the combination of the examination of the twins with family research, the author having procured data concerning close relatives, siblings, half-siblings, and parents and determined the morbidity-risks.

He has also procured data concerning consanguineous marriages and made an investigation of fertility. In the very concentrated preliminary report the author has not given any detailed account of the way in which the material has been collected or what guarantees he may have that there is no excess of concordant twins.

Concerning the author's results, special attention may be drawn to the following points: analysis of the age-corrected expectancy rates indicates that the chance of developing psychosis increases in proportion to the degree of blood relationship to the respective type of index case. The schizophrenia rates are 14.5 ± 1.72 per cent for the dizygotic co-twins; 86.2 ± 2.66 per cent for the monozygotic co-twins of the index cases. The corresponding rates with respect to manic-depressive psychosis are 26.3 ± 7.14 per cent for the dizygotic co-twins; 95.7 ± 4.23 per cent for the monozygotic co-twins. The expectancy of senile psychosis is 8.0 ± 5.42

per cent for the dizygotic co-twins; 42.8 ± 13.21 per cent for the monozygotic co-twins of senile twin index cases.

In judging the incidence of schizophrenia found by the author, it must be borne in mind that he gives the concept of schizophrenia a much wider application than it is given in European literature. He considers as schizophrenia, for instance, the "acute confusional states precipitated by extreme stress and the 'panneurotic' borderline cases without delusions or hallucinations."

A comprehensive psychiatric study on twins has been published by Slater.²⁸ This investigation is based upon a mental hospital population. In 364 patients it was ascertained that there had been a twin. After excluding the cases in which the twin partner had failed to reach adult life, 297 remained. Of these, 266 were personally examined by the author, and of the twin partners, 156. Fifty-one more cases were examined by a psychiatric social worker. The author has taken pains to get, as far as possible, an unbiased sample.

The clinical material comprised 67 uniovular and 224 binovular pairs and six pairs of doubtful ovularity. The proportion of uniovular twins (24 per cent) is according to expectation. The diagnosis uniovularity has been confirmed by detailed anthropological and fingerprint examinations. An interesting statistical analysis of the latter has been made. The examinations of twins have been supplemented by family research. The parents, siblings and children of the *propositi* have also been examined. Out of 297 pairs, there were 158 schizophrenic patients. There were affective disorders in 38 cases, involutional depressions in 11, epilepsy and organic psychosis in 49. A psychopathic and neurotic group included 52 cases. The author analyzes a number of different environmental factors. Unfortunately, the material is too brief, with a few exceptions, to allow for any definite conclusions on the basis of significant differences.

Among the more important results may be mentioned that he finds a concordance among schizophrenic uniovular twins amounting to 76 per cent. Among the binovular schizophrenic twins, 14 per cent were concordant. The incidence of schizophrenia among the siblings was five per cent. The author's analysis in connection with detailed case histories often throw interesting light upon the nature-nurture problem.

An interesting twin-family study of susceptibility to poliomyelitis has been published by Herndon and Jennings.¹⁸ An unselected series of 3890 reported cases of poliomyelitis was searched for twins. Forty-six families containing twins or triplets were located, one or more having had paralytic poliomyelitis while living with the twin partner. Test factors are presented for all the available members of the 46 families, including blood-group tests and taste tests. The authors diagnose 14 monozygotic and 31 dizygotic

twins. With regard to the paralytic form of poliomyelitis, twin pair concordance was found in 36 per cent of 14 monozygotic pairs and six per cent of dizygotic pairs. The difference is statistically significant. The authors conclude that the existence of a genetic factor controlling, at least in part, susceptibility to the paralytic form of poliomyelitis has been demonstrated.

REFERENCES

- ¹ Alström, C. H.: A study of epilepsy in its clinical, social and genetic aspects. *Acta psychiat. et neurol. Scandinav. suppl. 63*: 1950.
- ² Åmark, C.: A study in alcoholism. Clinical, social-psychiatric and genetic investigations. *Acta psychiat. et neurol. Scandinav. suppl. 70*: 1951.
- ³ Bleuler, M. mit Beiträgen von Baer, H., Condrau, G., Jacobs, D. I., Knoepfel, H. K., Stoll, W., Wipf, H., Wolf, D., and Züblin, W.: Untersuchungen aus dem Grenzgebiet zwischen Psychopathologie und Endokrinologie. *Arch. f. Psychiat. 180*:271-528, 1948.
- ⁴ Bökk, J. A.: The frequency of cousin marriages in three north Swedish parishes. *Hereditas. 34*:252-255, 1948.
- ⁵ —: Clinical and genetical entities in human populations with some remarks on schizophrenia, manic-depressive psychosis and mental deficiency in a north Swedish population. *Cold Spring Harbor Symposia on Quantitative Biology. 15*:123-128, 1950.
- ⁶ Borberg, A.: Clinical and Genetic Investigations into Tuberous Sclerosis and Recklinghausen's Neurofibromatosis. Diss., Copenhagen, Ejnar Munksgaard, 1951.
- ⁷ Brandt, S.: Werdnig-Hoffmann's Infantile Progressive Muscular Atrophy. Diss., Copenhagen, Ejnar Munksgaard, 1950.
- ⁸ Bremer, J.: A social psychiatric investigation of a small community in northern Norway. *Acta psychiat. et neurol. Scandinav. suppl. 62*: 1951.
- ⁹ Denny-Brown, D.: Hereditary sensory radicular neuropathy. *J. Neurol., Neurosurg. & Psychiat. 14*:237-252, 1951.
- ¹⁰ Ekblad, M.: A psychiatric and sociologic study of a series of Swedish naval conscripts. *Acta psychiat. et neurol. Scandinav. suppl. 49*: 1948.
- ¹¹ Hallgren, B.: Specific dyslexia ("congenital word-blindness"). A clinical and genetic study. *Acta psychiat. et neurol. Scandinav. 65*: 1950.
- ¹² Hanhart, E.: On a large Swiss family with simple recessive progressive muscular dystrophy (Duchenne-Griesinger's type). *Proceedings of the Eighth International Congress of Genetics. Hereditas. suppl. 586-588*, 1949.
- ¹³ Herndon, C. N. and Jennings, R. G.: A twin-family study of susceptibility to poliomyelitis. *Am. J. Human Genet. 3*:17-46, 1951.
- ¹⁴ Kallmann, F. J.: The Genetics of Psychoses. An Analysis of 1,232 Twin Index Families. *Congrès international de psychiatrie, Paris 1950, 6*:1-40 (*Actualités sci. et ind.* 1101). Paris 1950.
- ¹⁵ Kemp, T.: *Genetics and Disease*. Copenhagen, Ejnar Munksgaard, 1951.
- ¹⁶ Lennox, W. G.: The heredity of epilepsy as told by relatives and twins. *J.A.M.A. 146*:529-536, 1951.
- ¹⁷ Levison, H.: *Dystrophia musculorum progressiva*. Clinical and diagnostic criteria inheritance. *Acta psychiat. et neurol. Scandinav. suppl. 76*: 1951.
- ¹⁸ Mayer-Gross, W.: Mental health survey in a rural area. *Eugenics Rev. 40*:140-148, 1948.

- ¹⁹ Mjones, H.: Paralysis Agitans. A clinical and genetic study. *Acta psychiat. et neurol. Scandinav. suppl.* 54: 1949.
- ²⁰ Patterson, R. M., Bagchi, B. K., and Test, A.: The prediction of Huntington's chorea. An electroencephalographic and genetic study. *Am. J. Psychiat.* 104: 786-797, 1948.
- ²¹ Penrose, L. S.: *The Biology of Mental Defect*. London, Sidgwick & Jackson, 1949.
- ²² Price, B.: Primary biases in twin studies; A review of prenatal and natal difference-producing factors in monozygotic pairs. *Am. J. Human Genet.* 2:293-352, 1950.
- ²³ Roberts, J. A. F.: *The Genetics of Oligophrenia*. Congrès international de psychiatrie, Paris 1950, 6:55-117 (*Actualités sci. et ind.* 1101). Paris 1950.
- ²⁴ Schut, J. W.: Hereditary Ataxia; A survey of certain clinical, pathologic and genetic features with linkage data on five additional hereditary factors. *Am. J. Human Genet.* 3:93-110, 1951.
- ²⁵ Sjögren, T.: Genetic-statistical and psychiatric investigations of a west Swedish population. *Acta psychiat. et neurol. Scandinav. suppl.* 52: 1948.
- ²⁶ —: Hereditary congenital spinocerebellar ataxia accompanied by congenital cataract and oligophrenia. *Confinia neurol.* 10:293-308, 1950.
- ²⁷ — and Larsson, T.: Microphthalmos and anophthalmos with or without coincident oligophrenia. *Acta psychiat. et neurol. Scandinav. suppl.* 56: 1949.
- ²⁸ Slater, E. (with the assistance of James Shields): *An Investigation into Psychotic and Neurotic Twins*. Institute of Psychiatry, University of London, 1951.
- ²⁹ Stephens, F. E. and Tyler, F. H.: Studies in disorders of muscle. V. The inheritance of childhood progressive muscular dystrophy in 33 kindreds. *Am. J. Human Genet.* 3:111-125, 1951.
- ³⁰ Stern, C.: *Principles of Human Genetics*. San Francisco, W. H. Freeman & Company, 1949.
- ³¹ Strömberg, E.: Statistical and Genetical Population Studies within Psychiatry. Methods and Principal Results. Congrès international de psychiatrie, Paris 1950, 6:155-192 (*Actualités sci. et ind.* 1101). Paris 1950.
- ³² Thomsen, E.: Myotonia. Thomsen's Disease. Paramyotonia. *Dystrophia Myotonica*. Diss. Aarhus, Universitetsforlaget i Aarhus, 1948.
- ³³ Verschuër, O. von: Die Zwillingsforschung als Methode der Genetik vom Menschen. Bollettino del comitato internazionale per l'unificazione dei metodi e per la sintesi in antropologia eugenica e biologia (S.A.S.) 19:1-80, 1949.
- ³⁴ Welander, L.: Myopathia distalis tarda hereditaria. *Acta med. Scandinav. suppl.* 265: 1951.

Mental Hygiene

By HERBERT FREED, M.D.

PUBLIC ATTITUDES

THERE is agreement by both a psychiatrist⁵ and the lay medical editor¹⁰ of *News Week Magazine* that public education in psychiatry is not only desirable but necessary. After reviewing twice as many books in psychiatry as in any other field in the last five years, and maintaining her large correspondence in this same period, Clark concluded that psychiatry is the only branch of medicine in which the layman follows the literature consistently. All classes of the population should be enlightened using simple language without jargon while attempting to raise as little anxiety and guilt as possible.^{4, 41} The psychiatrist is told: "Be human and share your experience so we know what you really are . . . get into the same human boat with the rest of us if we are all to keep afloat."⁶

There seems to be an increasing need to change the attitude of the lawyers as a professional group toward psychiatry. In a carefully organized and controlled poll in Louisville, Kentucky³⁴ it was found that lawyers, of all the professional groups, showed the least faith in the efficacy of psychiatry. This deserves special consideration because their stand is of vital importance in regard to future improvements in our mental hospitals. Lawyers constitute the vast majority of our state legislators and administrators.

Films concerned with mental health "can and should be used" for general education with properly trained discussants to direct discussion.^{18, 39}

MENTAL HEALTH AND THE SCHOOLS

The Midcentury White House Conference on Children and Youth held December 4-7, 1950 sought to "study the ways in which the home, the school, the church, the law, welfare agencies and other social institutions are serving the needs of children."³⁸ The study of the achievements and future goals of our schools was well formulated in the 1950 yearbook of the National Education Association.¹⁹ The excellence of this volume is attested to not only by its varied contents but also by the recognition of the yearbook committee that perhaps the most important area in the personal well being of the school child omitted for discussion was the mental

health of the teacher, which they feel may well be the primary factor in the school's contribution to the wholesome development of children. Efforts at helping teachers to appreciate the emotional problems in children are reported¹⁷ with the utilization of the Delaware plan to "Teach Children How to Live" organized by H. E. Bullis.²² After seeing as their main goal the development of awareness among students regarding their feelings they set up a second objective which they ultimately realized was to develop therapists, carefully disguised as school teachers. They soon discovered this was a mirage and that, as Bullis had recently stated, teachers could not and should not be therapists. They did conclude that the classroom was an ideal setting for the development of sound mental health principles but disagreed with Bullis by stating there must be parallel teaching for the participating teacher and her supervisors. The inclusion of the parents became particularly evident after some teachers stated, "The parents say this course is just a method of getting the children to tell some of the household secrets."

Since mental hygiene as utilized in preventive psychiatry has the chief goal in the prevention of mental and emotional illness by the use of technics which influence large groups, an ideal area is available in the primary and secondary schools.²² Four projects which attempt to influence the mental health of the child through direct experiences in the classroom are discussed.

The Bullis project, probably the one most widely known and used in various school systems, utilizes a textbook with lesson plans dealing with common emotional experiences which teach a moral for improving human relations. While the theoretic strength of the course lies in strengthening the superego, the clinical value lies in the observation that one-sixth of the class ordinarily excluded from activities and discussions because of shyness became more socially active.

The "Force" project aimed at improving the skills of adolescents in social behavior and realistically approaching problems of love, marriage and parenthood also is dependent on enlarging the ego span through identification with the talented teacher as well as lessening superego severity through the latter's tolerance and acceptance.

The Ojemann project is probably the most ambitious in scope in that it does not aim at the inclusion of a course in the curriculum but at the revision of all texts and materials used in the schools which are concerned with behavior. Recognizing the great importance of the attitude of the teacher and the considerable time spent in training the teachers, its methods are based "on the assumption that the child can know and appreciate basic psychodynamic concepts."

The Forest Hill Village Project is another ambitious effort to train teachers and educate parents as well as conduct human relations classes in

grades 6 to 12. In these classes free discussion is allowed on topics that are chosen by the group with the instructor assuming a non-directive role. This would seem to be group therapy in a research frame of reference. As the committee on Preventive Psychiatry states, "This report will have succeeded if it assists in orienting educator and psychiatrist alike to certain trends in education of importance for healthy personality development." This seems all the more significant in light of the fact that the 1950 year-book of the National Education Association mentioned above does not have a single reference to any of these four projects. "Teaching is psychotherapy and psychotherapy is teaching" is a recurrent theme in the psychiatric literature this year.^{11, 14}

One cannot drop the topic of the importance of the attitude of the teacher in fostering mental hygiene without referring to the "Symposium on the Healthy Personality",²⁵ where the point was made by Colonel Bullis that applied research should be started immediately on the extremely serious problem "How can the prestige of teachers be raised in this country?"

FUNCTIONS OF THE MENTAL HYGIENE CLINIC

The contribution of the mental hygiene clinic to its community was made the topic for a roundtable discussion. Gardner expressed concern over the "increasing inability or unwillingness on the part of the clinics to assume and extend their responsibilities as social and health agencies in and of the community"; Coleman took the position that "the clinic must maintain the integrity of its nuclear function of treatment if it is to continue to have a reason for existence." Barhash pointed out that it was often the very lack of fundamental treatment skills which made many of the inadequate clinics develop ambitious plans to foster educational mental hygiene programs as a compensatory measure rather than treat sick children. A subtle undertone was crystallized by still another discussant who suggested that it should be determined whether preventive psychiatry is possible at all and to what extent it would consist of such measures as public education.^{18, 20, 21} State and local Mental Hygiene Societies expressed themselves much more optimistically about the future of preventive psychiatry.^{1, 53} They stressed assumption of responsibility and leadership by the non-psychiatric personnel with the psychiatrist leading by indirection.

The mental health planning in Israel is a provocative contrast to a questioning attitude as to whether preventive psychiatry is possible. Alt² states, "Children enjoy first priority in everyone's thoughts and feelings. The child is identified with the future of the State and is the focus of social planning." As an American observer he felt most impressed with the apparent clarity of goals for children in Israel and the more direct relationship between goals and the methods employed to achieve them. "Measures

which safeguard the security and well being of all children must take precedence over those for treatment of children with special problems. For the majority healing must come through opportunities for a fuller and happier life and satisfying human relationships, rather than through specialized therapy."

One frankly experimental approach to this problem is described⁹ in which instead of waiting for patients already aware of their illness and seeking help, the clinic chooses its clients according to its own criteria. Beside the direct work with parents, however, the infiltration of mental hygiene concepts through the medium of various professional workers such as the "madrick" is of extreme importance. He is a person who embodies the ideals of life in the "kibbitzim." These are the cooperative agricultural settlements where the children are reared through communal care. While less than 15 per cent of the inhabitants now live in these settlements, because of the rapid influx of immigrants the influence of the kibbitz on child education and child rearing remains dominant in the ideology of the nation. Alt concluded that "the extent of serious emotional difficulties among children is less in Israel than in our urban communities. At the same time considering the deprivations to which these young people and children have been exposed, it is fair to assume that psychological difficulties may exist at a deep level." He asked searchingly, "How far has the prevailing personal and social idealism either masked psychological symptoms or afforded so much support that people are able to function with relative adequacy?" In a thorough report on "Maternal Care and Mental Health," Bowlby⁸ suggests that the kibbitz provides an unusually rich opportunity for research in child development which should not be missed. He notes that there seems to be a trend toward parents steadily demanding more responsibility in the rearing of their children in these communal settlements.

WHAT IS NORMALITY?

In a discussion that is marked by its knowledge of sociology rather than of psychiatry, Eaton¹³ emphasizes the fact that the social sciences have no generally accepted criterion of mental health. He concludes: "Mental health cannot be reduced to such a single dimension. It is a value judgment with all the potentialities for variation and change implicit in such a relationistic entity." In this formulation he shows a measure of agreement with Dr. John Whitehorn in his 1951 Presidential address⁵² who said, "As psychiatrists we have come to focus special attention upon the importance of shared values and the communicability of value judgment, as the basis of the healthy and enthusiastic life of man as an inherently social being." When he later emphasized that we should seek a better understanding of the "factors that hinder and the factors that promote the sharing of emo-

tional values" he was touching upon the technic of communication. This became the topic of a stimulating book⁴⁶ which is the fruit of the collaboration of a psychiatrist and an anthropologist. It is not only concrete evidence of the growing interdisciplinary productivity³ but also the timely manifestation of the psychiatrist's determination to question the scientific basis of the various schools of therapy. Workers in the field of mental hygiene will find it difficult to disagree with their observation: "Some of the confusion existing in psychiatry today is clearly related to the improper use of a rather nebulous concept of normality." More attention is being given to the concept of the normal and also to that of the optimal in mental health.^{31, 49}

PANIC CONTROL AND MENTOCIDE

At the Midcentury White House Conference,³³ war and the defenses against it were in the forefront of the thinking of many delegates. If the most important security we can provide for our children is the security against physical annihilation we can aid through the psychiatric aspects of civil defense.²³ Panic control is amply discussed in additional reports.^{16, 36, 51} The emotional stress resulting from air war is covered in a new monograph²⁶ which suggests that we can predict the psychologic consequences of atomic warfare since the psychologic responses resulting from the atomic bomb disasters generally do not differ in any unique way from those produced by other types of bombing disasters.

But physical annihilation of a national group may take second place to "Mentocide."³⁷ This is defined as an organized system of psychologic intervention and judicial perversion, in which a powerful tyrant synthetically injects his own thoughts and words into the minds and mouths of the victims he plans to destroy by mock trial. The author points out that new child rearing attitudes to make for stronger egos are necessary for future protection but that now we must formulate our psychiatric standpoint toward this challenge. Experimental evidence corroborating some of Meerloo's hypotheses was reported by other observers.⁴⁵ Margaret Mead³⁵ suggests that these new child rearing attitudes are already present in the young veterans of World War II where we see a new form of parenthood with a prevailing mood, not of anxiety, but of awareness.

There is increasing discussion about social psychiatry with at least one psychiatrist pessimistic about its future because of the attitude of the legal profession.⁴⁰ From the perspective of the sociologist⁴² the role of the psychiatrist is well defined. Dunn¹² feeling that the complexities of modern life has threatened the patient-doctor relationship, has advocated that we seek out all possible mental health opportunities in the general hospital to re-establish good feeling. Finally, the war has forced upon us a consideration of the psychosocial dynamics of mobility.⁵⁰

INDUSTRY AND THE AGED

The problems of the aged confronted by forced retirement by the wish to remain emotionally secure with rapidly changing physical and environmental conditions were focused upon in the Second International Gerontological Congress held in St. Louis, September, 1951.^{28, 29, 54} A provocative forecast was made that the oversupply of enforced leisure and increased mobility of older people may result in "boom towns of the aged."⁴⁴

Industry has also become increasingly cognizant of the alteration in manpower potentials as well as the need for improved human relations.^{24, 27, 32} It is suggested that the overage employee be trained for retirement.⁴⁷ While many authorities insist that work is not a precipitating factor in the development of emotional disturbances, a psychoanalytic discussion of the psychic trauma resulting from mass production is formulated.⁴³ The author is particularly interested in showing the way the infantile conditioning of individuals is reenforced by their working conditions; the development of passivity is fostered as well as the pressures of hostility and anxiety increased. This makes the worker more susceptible to the wiles of the demagogue.

Infiltration of the principles of mental hygiene by working with the executives and supervisors in large industrial organizations is bearing fruit. Four years of experience in an employee health program attached to the T.V.A. is outlined.³³ The Federal Security Agency, determined to increase the effectiveness of its executives in interpersonal situations successfully, tried to bring about increased self understanding through group analysis.³⁰ Despite the many limitations of applicability of this type of "treatment" to "successful" people the results proved so satisfactory that the project will be continued. It is particularly recommended where an investment in personnel on a long-range basis is considered worthwhile.

SUGGESTIONS FOR THE FUTURE

Suggestions were made that we establish a citizens committee for children with both professional and lay representation for sound long-range integrated planning on a state-wide basis for the total needs of all children—whether sick or well⁴⁸ and that we have a routine mental health examination for children in the schools analogous to the physical examination now given.¹⁵ While most observers consider the event of the year to be the Fourth International Mental Health Congress, held in Mexico in December, 1951, they are still keeping a weather eye on the significance of "Blondie"⁷⁷ the comic book—the new venture in education for Mental Health which became available for national distribution in January, 1951.

REFERENCES

- ¹ Aukes, I. and Novick, R. G.: Professional responsibility for community mental health. *Ment. Hyg.* 35:432-438, 1951.
- ² Alt, H.: Indications for mental health planning for children in Israel. *Am. J. Orthopsychiat.* 21:105-123, 1951.
- ³ Bartemeier, L. H.: Psychiatry and international understanding. *Am. J. Psychiat.* 107:641-643, 1951.
- ⁴ Baumgartner, L.: Psychiatry and the child health services. *Am. J. Orthopsychiat.* 21:693-706, 1951.
- ⁵ Binger, C.: Public education in psychiatry. *Am. J. Psychotherapy.* 5:4-15, 1951.
- ⁶ Bingham, J.: What the public thinks of psychiatry. *Am. J. Psychiat.* 107:599-601, 1951.
- ⁷ Blondie—A comic book. New York National Association for Mental Health, 1951.
- ⁸ Bowlby, J.: Maternal care and mental health. *Bull. World Health Organization.* 3:355-533, 1951.
- ⁹ Caplan, G.: Public health approach to child psychiatry. *Ment. Hyg.* 35:236-248, 1951.
- ¹⁰ Clark, M.: Popularization of psychiatry. *Am. J. Psychotherapy.* 5:16-23, 1951.
- ¹¹ Clothier, F.: Education for mental health. *Ment. Hyg.* 35:560-570, 1951.
- ¹² Dunn, W. J.: Mental-health opportunities in the general hospital. *Ment. Hyg.* 35:190-198, 1951.
- ¹³ Eaton, J. W.: The assessment of mental health. *Am. J. Psychiat.* 108:81-90, 1951.
- ¹⁴ Editorial: Mental health education. *Am. J. Psychiat.* 107:552-553, 1951.
- ¹⁵ Fabian, A. A. and Holden, M. A.: Treatment of childhood schizophrenia in a child guidance clinic. *Am. J. Orthopsychiat.* 21:571-583, 1951.
- ¹⁶ Fantl, K.: Psychiatric aspects of civilian defense. *Am. J. Psychiat.* 107:488-492, 1951.
- ¹⁷ Farmer, H. and Rossman, W. B.: Helping teachers appreciate emotional problems in children. *Am. J. Psychiat.* 108:374-380, 1951.
- ¹⁸ Felix, R. H.: Mental hygiene as public health practice. *Am. J. Orthopsychiat.* 21:707-716, 1951.
- ¹⁹ Fostering mental health in our schools, Washington, D. C., National Education A. 1950.
- ²⁰ Frankl, G.: Community psychiatry and its organizational problems. *Ment. Hyg.* 35:532-539, 1951.
- ²¹ Gardner, G. E., Coleman, J. V., Barhash, A. Z., et al: Appraising the contribution of the mental hygiene clinic to its community. *A. M. J. Orthopsychiat.* 21:74-104, 1951.
- ²² Report No. 18. Group for the advancement of psychiatry. Promotion of mental health in primary and secondary schools. Jan. 1951.
- ²³ Report No. 19. An introduction to the psychiatric aspects of civil defense. April, 1951.
- ²⁴ Report No. 20. The application of psychiatry to industry. July, 1951.
- ²⁵ Jahoda, M.: Toward a social psychology of mental health. In Senn, M. (ed.) *Symposium on the Healthy Personality.* New York, Josiah Macy Jr. Foundation, 1950.
- ²⁶ Janis, I. J.: *Air War and Emotional Stress.* New York, McGraw Hill, 1951.
- ²⁷ Johnson, G. S.: Is a compulsory retirement age ever justified. *J. Gerontol.* 6:263-271, 1951.

- ²⁸ Program of Second International Gerontological Congress. *J. Gerontol.* 6: Suppl., 51-171, 1951.
- ²⁹ Kleemeier, R. W.: Work program and adjustment in old age. *J. Gerontol.* 6:372-379, 1951.
- ³⁰ Laughlin, H. P. and Hall, M.: Psychiatry for executives. *Am. J. Psychiat.* 107:493-497, 1951.
- ³¹ Lemkau, P. B.: The future organization of psychiatric care. *Psychiatric Quart.* 25:201-212, 1951.
- ³² Line, W.: Human relations in industry—A systematic challenge. *Brit. J. Med. Psychol.* 23:42-48, 1951.
- ³³ McAtee, O. B.: The establishment and function of an industrial mental hygiene service. *Am. J. Psychiat.* 107:623-627, 1951.
- ³⁴ Maisel, A.: When would you consult a psychiatrist? *Colliers Magazine*, May 12, p. 13, 1951.
- ³⁵ Mead, M. and Macgregor, F. C.: *Growth and Culture*. New York, G. P. Putnam's Sons, 1951.
- ³⁶ Meerloo, J. A. M.: First aid in acute panic states. *Am. J. Psychotherapy.* 5:367-371, 1951.
- ³⁷ —: The crime of menticide. *Am. J. Psychiat.* 107:594-598, 1951.
- ³⁸ Midcentury White House Conference on Children and Youth. *Child.* 15:106-119, 1951.
- ³⁹ Middlewood, E.: Mental health films in community education. *Am. J. Orthopsychiat.* 21:47-53, 1951.
- ⁴⁰ Miller, E.: Is a social psychiatry possible? *Brit. J. Med. Psychol.* 23:213-219, 1951.
- ⁴¹ Newell, H. W.: Fulfilling our purposes. *Am. J. Orthopsychiat.* 21:445-451, 1951.
- ⁴² Parson, T.: Illness and the role of the physician. *Am. J. Orthopsychiat.* 21:452-460, 1951.
- ⁴³ Pederson-Krag, C.: A psychoanalytic approach to mass production. *Psychoanalytic Quart.* 20:434-451, 1951.
- ⁴⁴ Randall, O. A.: Sociological aspects of Linn. *J.A.M.A.* 147:1325-1326, 1951.
- ⁴⁵ Redlich, F. C., Rant, L., and Session, C. H.: Narcoanalysis and truth. *Am. J. Psychol.* 107:586-593, 1951.
- ⁴⁶ Ruesch, J. and Bateson, C.: *Communication*. New York, W. W. Norton, 1951.
- ⁴⁷ Scheid, P. N.: Training the overage employee for retirement. *J.A.M.A.* 147:1323-1324, 1951.
- ⁴⁸ Senn, M. J. E.: After the Midcentury White House Conference—What? *Child.* 15:73-79, 1950.
- ⁴⁹ Smith, M. B.: Optima in mental health. *Psychiatry.* 13:503-510, 1950.
- ⁵⁰ Tyhurst, L.: Displacement and migration. *Am. J. Psychiat.* 107:561-568, 1951.
- ⁵¹ Waggoner, R. W. and Himler, L. E.: Psychiatric aspects of civilian defense. *J. Michigan M. Soc.* 50:278-281, 1951.
- ⁵² Whitehorn, J.: The individual psychiatrist and social psychiatry (Presidential Address) 108:1-6, 1951.
- ⁵³ Whitman, S.: Organization for mental health in local communities. *Ment. Hyg.* 35:618-631, 1951.
- ⁵⁴ Zeeman, F. D.: Constructive Programs for the mental health of the elderly. *Ment. Hyg.* 35:221-234, 1951.

Forensic Psychiatry

By WINFRED OVERHOLSER, M.D., Sc.D.

IN THE review of this subject for 1950, mention was made of the Draft Act Governing Hospitalization of the Mentally Ill, prepared by the Federal Security Agency and widely distributed throughout the country. Already this draft has borne fruit, in that Utah¹ and Idaho² have already passed legislation along the lines suggested. It may not be entirely fortuitous that several other States also, among them Illinois,^{2a} Indiana,³ Maine,⁴ Nevada,⁵ Pennsylvania,⁶ and Tennessee,⁷ revised their laws regarding admission to mental hospitals. The Draft Act was discussed at length by Whitmore,⁸ and a general discussion of the proper criteria for such legislation is found in an article by Melaney⁹ with the subtitle "Treatment or Travesty." One is moved to suggest that the legal profession is showing greater interest in more humanity and less legalism when it comes to legislation of this type. Perhaps some day even Texas and Alaska will cease to require jury trial for commitment!

Roche¹⁰ presents an interesting discussion of expert testimony, with particular reference to the perils of making psychiatric diagnoses (and especially that of "psychopathic personality") at a distance, i.e., without examination of the patient, and Challener¹¹ presents some of the problems of expert testimony, notably those due to bias and partisanship. He urges the enactment of the Uniform Expert Testimony Act, which although proposed in 1937, has not yet been adopted even in part by more than two states.

The Briggs Law of Massachusetts came to the attention of the United States Circuit Court of Appeals,¹² and the State court was sustained in ruling that a defendant examined under that law is not entitled as a matter of right to further psychiatric examination at public expense.

Two articles on the "tests" of criminal responsibility appeared, (Cornette¹³ and Rexroad¹⁴) both by attorneys and both in favor of modernization and widening of the existing criteria.

Bennett¹⁵ discusses accident-proneness in multiple sclerosis. He points out that the euphoria of the patient and the insidiousness of the symptoms often mask the fact that the injury is often the result, rather than the cause,

of the disease. The failure of workmen's compensation tribunals to understand the course of the disease is largely responsible for the large "sympathetic" verdicts not infrequently allowed. He recommends impartial expert witnesses as a possible preventive of such unwarranted awards.

Crawfis,¹⁶ in an article on privileged communications, notes that only about one half of the States (New York being the first in 1828) have statutes relative to privileged communications made to physicians.

Hubert Winston Smith¹⁷ studies in scholarly detail the technic and desiderata (from the lawyer's point of view) of cross examination of psychiatric and neurologic testimony in personal injury cases.

An article by Orenstein¹⁸ and an unsigned note in the *Indiana Law Journal*¹⁹ emphasize the importance of the psychiatric examination of the complaining witness in certain rape cases in which corroborative evidence is slight or non-existent. The Nebraska Supreme Court pointed out 30 years ago (as did Lord Coke long before) that "public sentiment seems inclined to believe a man guilty of any illicit sexual offense he may be charged with." Both articles cite cases in which innocent men were convicted on the unsupported statements of mentally defective or otherwise disordered girls.

A report of the Société Internationale de Criminologie²⁰ (February 15, 1951) is devoted to narcosis and its judicial uses. The reporter, Professor Jean Lhermitte, favors the use of narcotics such as pentothal *only* for the determination of malingering (narco-diagnostic) but not for use in obtaining information as to the guilt of the accused (narco-analysis). The paper was discussed by Professors Delay and Heuyer, and by several lawyers.

The Monograph Series of the World Health Organization was inaugurated with a study of Psychiatric Aspects of Juvenile Delinquency, by the late Lucien Bovet.²¹

The interest in "sexual psychopath" legislation mentioned a year ago continues. Guttmacher's "Gimbel Lectures on Sex Offenses" (Norton 1950) is a thoughtful study of the problem, as is an article by Bowman.²² Both point out some of the gaps in our knowledge as to the type of offender and the proper treatment and the need for research. California has recently authorized a thorough-going study of this whole subject.²³ An extended report has been issued by the Michigan Governor's Study Commission on the Deviated Criminal Sex Offender.²⁴ Professor Paul Tappan²⁵ describes the treatment of the sex offender in Denmark; there in certain cases castration is employed. Nearer home, Hawke²⁶ gives a review of 330 cases of castration, recommending it as controlling (!) masturbation and perversion.

Karpman,²⁷ in discussing sexual psychopathy, concludes that the term has no proper place in the nomenclature. He urges sex education in childhood and emphasizes the fact that the disorders generally included in the term are in many cases amenable to psychotherapy. In the legal literature,

articles on the subject by Schlesinger and Scanlon,²⁸ Judge Hoffman of Chicago,²⁹ and Prewett³⁰ may be mentioned. A recent Missouri decision upholds the "sexual psychopath" statute of that State.^{30a}

Abrahamsen³¹ presents the results of his Sing Sing study of sex offenders. He found four groups—violent and untreatable (15 per cent), untreatable at present (35 per cent), treatable in hospital (40 per cent), and treatable on an out-patient basis (10 per cent).

Most of the State legislatures met in 1951, with the usual resulting flood of legislation. Iowa³² changed the name of its State hospitals to mental health institutes. Maine³³ pointed the way to closer interstate cooperation by authorizing a Tri-State Authority (subject to the concurrence of New Hampshire and Vermont) for the institutional care of defective delinquents.

Georgia³⁴ joined the list of States recognizing "incurable insanity" as a ground for divorce. Minnesota³⁵ established an Interim Commission on Alcoholism.

Some of the books of interest have already been mentioned. One other should be recommended—a readable, informative volume, social in its approach despite the title, by an experienced jurist. It is entitled *Sex and the Law* (Prentice-Hall, 1951), by Judge Morris Ploscowe.

REFERENCES

- ¹ Ch. 113, Laws of 1951.
- ² Ch. 290, Session Laws of 1951.
- ^{2a} House Bill 234, approved July 16, 1951; page 1585, Sessions Laws of 1951.
- ³ Ch. 181, Acts of 1951.
- ⁴ Ch. 374, Acts of 1951.
- ⁵ Ch. 331, Statutes of 1951.
- ⁶ Act No. 141, Laws of 1951.
- ⁷ Ch. 114, Pub. Acts of 1951.
- ⁸ 19 Geo Wash. U.L.R. 512-530, 1951.
- ⁹ 12 U. of Pittsburgh L.R. 52-72, 1950.
- ¹⁰ 22 Pa. Bar Assoc. Quart. 140-153, 1951.
- ¹¹ 22 Pa. Bar Assoc. Quart. 304-316, 1951.
- ¹² McGarty v. O'Brien, 188 F. 2nd 151. Abstracted in J.A.M.A. 147:895, 1951.
- ¹³ 39 Ky. L.J. 463-9, 1951.
- ¹⁴ 19 J. Bar Assoc. Kansas 125-128, 1950.
- ¹⁵ Bennett, A. E.: Accident proneness in multiple sclerosis; relationship to trauma, with medico-legal implications. J. Nerv. & Ment. Dis. 113:198-210, 1951.
- ¹⁶ Crawfis, E. H.: The physician and privileged communications as they relate to mental state. Ohio State M. J. 46:1082-1085, 1950.
- ¹⁷ 4 Vanderbilt L.R. 1-62, 1950.
- ¹⁸ Orenstein, Leo L.: Examination of the complaining witness in a criminal court. Am. J. Psychiat. 107:684-688, 1951.
- ¹⁹ 26 Indiana L.J. 98-103, 1950.
- ²⁰ Report of the Société Internationale de Criminologie (February 15, 1951). J. Pinatel, Secy., 28, Ace. de Friedland, Paris VIII France.

- ²¹ Bovet, Lucien: Psychiatric Aspects of Juvenile Delinquency. Monograph Series 1, Geneva, World Health Organization, 1951.
- ²² Bowman, K. M.: The problem of the sex offender. *Am. J. Psychiat.* 108:250-257, 1951.
- ²³ Report, Commission on Sex Offenders. Sacramento, Progress Report of Assembly Interim Committee on Judicial System and Judicial Process, pp. 103-170, 1951.
- ²⁴ Thurber, D.: Governor's Study Commission on the Deviated Criminal Sex Offender. Michigan, 1951.
- ²⁵ Tappan, Paul W.: Treatment of the sex offender in Denmark. *Am. J. Psychiat.* 108:241-249, 1951.
- ²⁶ Hawke, C. C.: Castration and sex crimes. *Am. J. Ment. Deficiency.* 55:220-226, 1950.
- ²⁷ Karpman, Ben: The sexual psychopath. *J.A.M.A.* 146:721-726, 1951.
- ²⁸ 11 U. of Pittsburgh L.R. 636-654, 1950.
- ²⁹ 32 Chicago Bar Record 103-114, 1950.
- ³⁰ 5 Arkansas L.R. 214-216, 1951.
- ^{30a} State v. Green, 232 S.W. 2nd 897.
- ³¹ Federal Probation 14:26-32, 1950. See also extended report to Governor Dewey, Albany 1950.
- ³² Ch. 83, Acts of 1951.
- ³³ Ch. 387, Acts of 1951.
- ³⁴ No. 465, Acts of 1951.
- ³⁵ Ch. 406, Laws of 1951.

Criminal Psychopathology

By SYDNEY B. MAUGHS, M.D.

SCHMIDEBERG¹⁵ comments on the senselessness of continually sentencing habitual criminals. She says that they are unable to stop repeating crimes since they are motivated by unconscious factors. She feels that social help and psychiatric treatment should be given to psychopaths, "pre-delinquents," neurotics and other unstable persons at an early date. In addition, she would even extend financial, social and psychologic help to people who are under stress or in temporary difficulties. The need for constructive treatment in prison is pointed out but the author recognizes it is out of the question so long as there is only one psychiatrist per one thousand inmates. Treatment in prison should be followed by help or treatment after the individual has left prison and has to face a difficult reality. She calls attention to the well known (but too often neglected) fact that every habitual criminal is supported by society for the rest of his life; in prison by the tax-payer, out of prison by his victims. In modern hygienic prisons he is likely to live to a ripe old age. The moderate estimate of an habitual criminal's cost to society is at least \$50,000 if he lives to age 60. It is her belief that this money could be used more constructively.

Henderson⁸ in a memorandum submitted to the Royal Commission on Capital Punishment, states that the violent methods of punishment and retribution in vogue have little or no constructive value and make no contribution toward social reformation. He feels that one can never divorce the offense from the life history of the individual. He criticises the intellectualistic and moralistic point of view of the law and its lack of appreciation of the fact that conduct is motivated by instinctive drives. Although recognizing that the medical point of view is criticised as too liberal, he feels that it is only by realizing that individualization is the dominant truth of modern medical science, whether applied to disease or crime, that we can look forward more hopefully to the future. He notes that it is rare for criminal conduct to be the first sign or indication of mental disorder. He would advise a psychiatric examination in every case involving capital punishment. The law is unjust in refusing to allow mental deficiency to be utilized as a defense. There should be good psychiatric units set up, where

satisfactory examination and observation can be carried out previous to trial and where suitable cases could have adequate treatment after trial.

Overholser¹² calls attention to the fact that Indiana and Washington have now enacted sexual psychopath laws. California has amended its law to provide for placement in a state hospital for not more than two years.

Guttmacher⁵ discusses the function of the adult court psychiatric clinic. There are eight such clinics in the country—two in Chicago, two in New York City, and one each in Detroit, Baltimore, Cleveland and Pittsburgh. All serve primarily criminal courts except the one in Chicago which serves the municipal or magistrate courts. The psychiatrist can offer much help to the court. The court psychiatric clinic practically puts an end to the battles of experts in criminal cases. He outlines the practical professional organization of the adult psychiatric court clinic for a city with a million people. Guttmacher, as the result of his experience as the head of this clinic in Baltimore, has come to realize that the legal leaders of this country must develop an understanding of—and trust in—psychiatry and psychiatrists before there is any hope for reforms so urgently needed in the problems of mental disorder and the law.

Haines⁶ feels that a complete psychiatric evaluation must be made on all youthful offenders and special attempts made to rehabilitate this group if there is to be an improvement of forensic psychiatry. He points out that there will continue to be difficulty in differentiating between insanity, i.e., irresponsibility in the legal sense, and mental illness in the medical sense. If we strive to do away with the insanity issue at the time of trial and have the individual tried for the offense, and then use psychiatry as a means of disposal and not as a means of defense, we eliminate much of the unfavorable impression of court psychiatry in the layman's mind. Psychiatry is now used as a defense and the guilt or innocence is not proved. Haines suggests the general enactment of legislation to provide for a panel of psychiatrists to be appointed by the court and made available to both sides; psychiatrists testifying in courts should have access to all information from both sides to avoid partiality and their fees should be paid by the State. He would abolish the hypothetical question and would keep the expert testimony of the psychiatrist along medical lines so far as it is humanly possible to do so. He urges that something be done to prevent the newspapers from glamorizing crime.

Cruvant et al.² comment on an institutional program for committed sex deviants. They conclude that their illnesses are psychodynamically determined but feel it is doubtful whether present technics are equal to the task of cure. More research is needed in all phases of this problem.

Patterson¹³ reports that group therapy conducted by an able individual has much to offer in a school for delinquent adolescent girls. Drama therapy

can also make a distinct contribution. However, neither group therapy nor drama therapy is a substitute for individualized therapy.

Cushing³ comes to the conclusion that the psychopathology of the sexual offender is not actually the psychopathology of an individual but the psychopathology of a culture. Sexual offenses, as we term them, are indeed stimulated, aided and abetted by our religious views, our cultural attitudes and our social structures. Penalties enforced are a defensive measure imposed by individuals whose inhibitions are outraged.

Williams¹⁷ reports on a study of 100 cases of men confined to naval disciplinary barracks. All had physical, psychiatric and psychologic examinations. Sixty-seven per cent were convicted of absence offenses while the others were convicted of more serious offenses. All had severe emotional difficulties and 3 per cent of the total were psychotic. He feels that this indicates that confinement is of questionable value unless a very intensive program of psychiatric treatment is possible during this period. Confinement alone appeared to make the man unfit for an adjustment in society because it increased the hostile-aggressive patterns followed from childhood. The goal of confinement should be to prepare the prisoner psychologically for an adjustment in society rather than increase his hatred for all authority.

Hawke⁷ submits studies on 330 cases of castration accumulated over nearly 50 years at the Kansas State Training School. The results demonstrated, according to the author, that castration improves the sex criminal sociologically in that he usually refrains from his anti-social acts and becomes an acceptable member of society. Psychologically he is stabilized, does not suffer any mental deterioration and while he may have a moderate degree of inferiority complex, this is favorably balanced by his social improvement. Physically he is a better organism. Hawke points out the fact that in no way is the castrate like our conception of a castrate, i.e.—the eunuch.

Reichard and Tillman¹⁴ report their conclusions from a study of a group of men who committed murder. All suffered from a state of extreme mental turmoil such as is frequently prodromal of a schizophrenic breakdown. The primary purpose of the murders was the discharge of pent-up hostility—the majority of these were characterized by unnecessary ferocity which went far beyond what would be required merely to kill a person. This feature was so striking that, whenever an assault is characterized by unnecessary ferocity, the authorities should raise the question of severe mental illness. The senselessness of the murders—most of them served no external goal—indicates that these crimes were primarily serving an internal need to discharge hostility. The victims were victims as the result of the mechanism of displacement of hostility. The murderers were strikingly calm after their acts and revealed no expression of remorse. This further supports the theory

that primary purpose of the act was the discharge of hostility regardless of whom the victim might be. That so many of these patients were found not to be obviously insane is evidence that the discharge of hostility afforded the ego relief from the threat of being overwhelmed by the id. Evidence also shows that sex is actually repulsive to such men. In fact, there may be an underlying basic hatred of the opposite sex. Lesser acts of violence may serve the same purpose. The authors' hypothesis in regard to the dynamics of schizophrenia is that "unassuageable anger," derived from early infantile frustrations, is an important etiologic factor leading to the outbreak of psychosis. Murder and suicide may on occasion serve as alternate channels of discharge and preserve the ego.

McDermaid and Winkler¹¹ made a study of 27 patients—20 male and seven female—charged with homicide or manslaughter. Fifteen males and one female were nonpsychotic and five males and six females psychotic. Environmental influences of a destructive nature were found in 13 of the 15 non-psychotic males. Organic factors were found in two other non-psychotic males. One patient showed schizoid features all his life and committed homicide in a state of pathologic intoxication. Only three of 15 non-psychotic male patients could be considered chronic delinquents and the majority had never been arrested before. There was chronic alcoholism in only four male cases. Suicidal tendencies were noted in four male cases. Suicidal tendencies were noted in four of the male non-psychotic patients and one of them made a serious suicidal attempt. Two of the male psychotic patients made suicidal attempts. Four of six female psychotic patients were suicidal and three of these made suicidal attempts. Four of the male psychotics were schizophrenics and one an involutional psychosis, paranoid type. In three of these five, homicidal action was related to the content of the delusion. The authors felt that mental deficiency is not a causative factor of homicide. Social factors play a provocative role only in persons who are disposed by their personality make-up. Psychoanalytic interpretations of delinquent behavior cannot be applied to the majority of murder cases. Homicidal action in most cases was considered as a defense reaction to an extreme anxiety state. The factor which caused the loss of the ego defenses remains unknown but may be found in some organic physico-chemical changes produced by the anxiety condition. When the authors evaluated the life history of the psychotic patients, they found that it is mainly the psychotic process which leads to a break with reality and causes the patient's abnormal behavior and his homicidal tendencies. Homicide is rarely the first manifestation of a psychotic disorder. The common motive in all cases of infanticide is the conscious feeling of inability to bring up the child and to take proper care of it. They concluded that, in a great number of cases, homicide is preventable by giving psychotherapy to psychoneurotic

patients with tendencies to anxiety states, by treating psychoneurotic children in child guidance clinics and relieving unfavorable social conditions by social service work in a mental hygiene clinic. Particular attention should be spent on mothers whose feelings of inadequacy with regard to their rearing of children, when combined with suicidal tendencies, may easily turn to infanticide.

Karpman¹⁰ reports the results of a roundtable discussion of the psychopathic delinquent child. In his own mind there is little doubt that the adult psychopathic individual is the vertical continuation of the psychopathic child. Lourie¹⁰ believes that the roots of psychopathy may be found in the first five years of life—a specific constitutional anlage, gene-determined. Rabinovitch,¹⁰ quoting Bender, feels that the condition appears whenever close child-adult relationships are not present during the first years, the critical age being under two. Out of this there develops an inability on the part of the infant to relate, that is, to establish adequate object relationships and, consequently, there is an absence of neurotic patterns. In normal, neurotic or schizophrenic children there is anxiety because of threats to object relationships. The psychopathic child has no anxiety because he has established no identification and is not motivated toward any. Spitz¹⁰ emphasizes the prominent role played by early separation from others—their (mother's) personality was such as to cause rapidly changing attitudes toward the children. Lippman¹⁰ found that in many juvenile psychopaths unrecognized attitudes toward the child by his parents were present during the first year of life which served to set him apart from the rest of the family. Karpman¹⁰ comments that all these findings suggest it would be of interest to analyze the parents, particularly mothers of these children. Spitz¹⁰ feels that unpredictable, rapidly changing mother attitude makes the establishment of reliable object relationships impossible in the first year. It seems to him that it is obvious that in the psychopathic child it is the mechanism of identification that is distorted. Karpman¹⁰ comments that this inconsistent mother with rapidly changing attitudes may explain the presence of psychopaths in economically favorable homes. Both Spitz¹⁰ and Bender feel that the formation of object relations is difficult and that this takes place before the age of two. Lourie¹⁰ points out early differences in language development and feels this delay is primary and that the resulting difficulty in forming relationships is secondary to this. The mechanism of projection, which usually diminishes after a recrudescence between the ages of one and a half and two, remains prominent throughout these children's later life. These children are actually uncomfortable when attempting to use fantasy. Allen¹⁰ agrees but would particularly emphasize the problem of projection. The child's ability to create irritation and anger in others enables him to sustain his projection that everyone is fighting him. He

feels that these patterns are modifiable. Almost all the participants agreed that the pathology lay within the ego of these children. It was suggested that the ego is lacking in its function of synthesis. Karpman¹⁰ summarizes as follows: "The chief etiological offender, on which there seems to be a good concurrence of opinion, appears to be a particular type of mother-infant relationship, resulting in disturbances of the processes of projection, objectification and identification. Out of this emerges the recognition that psychopathy in children can be treated and may perhaps be eradicated through education of parents."

Cruvant and Yochelson¹ comment on the extraordinary looseness with which the term "psychosis with psychopathic personality" seems to be used. A study of written opinions solicited from a number of colleagues, when contrasted with a number of cases so diagnosed, disclosed discrepancies between theory and practice. The authors feel that these discrepancies are due to factors operating within the psychiatrist in his role of "participant observer." They point out the interesting fact that in dealing with psychopaths the psychiatrist is confronted with the conflict of integrating his clinical judgment and his feelings of social responsibility. They conclude that it seems to them more handicapping than helpful at this time to consider "psychopathic personality" and "psychosis with psychopathic personality" as distinct entities rather than as varieties of the conventional neuroses and psychoses.

Kahn⁹ believes that only degree differentiates the manifestations of psychopathy from normal behavior. A multidimensional view must be established for diagnosis. Five points of view which may be used are the constitutional, structural, developmental, experiential and situational. Variants in the instinctual drives contribute to the make-up of the psychopathic person. Maldirection of development is important in the genesis of psychopathy. Precocity, retardation and other anomalies of development can evoke psychopathic behavior. Kahn considers these disturbances in the development of psychopathic personalities as evolutive anachronisms. The reaction of the person to a situation is normal when he makes what he can of it while adapting to it. The psychopath is apt to give more or less of himself than the normal person, tending to overestimate his own position in the situation.

Silverman¹⁶ reports on electroencephalographic findings in the psychopath. He points out that six independent investigators have reported on the electroencephalographs of psychopathic personalities. Of a total series of 694 psychopathic subjects, 336 or 48.4 per cent had clearly abnormal electroencephalographs. The most characteristic abnormality was a five to seven per second rhythm with maximum amplitude from the anterior

region of the scalp. Investigators who distinguish between aggressive and inadequate psychopathic personality found consistently many more abnormal electroencephalographs among the former. The implication of these findings is the existence of an organic factor in causation of the disorder. The evidence to date points toward an inborn and/or an early acquired defect. However, Silverman points out that the organic defect does not account for the entire psychopathic picture. In his cases, 80 per cent of the patients had clearly traumatic childhoods involving disturbed parent-child relationships. It is felt, then, that the cerebral defect serves to increase the sensitivity to the emotional trauma of childhood and may even facilitate the psychopathic choice of the neurotic pattern—the tendency to “act out” rather than to internalize the conflict. He feels that clinically these formulations have important implications. They should stimulate investigation of each such patient for the existence of organic lesions. They suggest research on the effect of drugs in controlling cerebral dysfunction and afford hope that psychopathic defect—if related to cortical immaturity—may mature and that with psychotherapy the total personality may also mature or follow a more normal pattern. He points to the need for reappraisal and change in the medico-legal handling of these cases.

REFERENCES

- ¹ Cruvant, Bernard A. and Yochelson, Leon: The psychiatrist and the psychotic psychopath. *Am. J. Psychiat.* 106:594, 1950.
- ² —, Meltzer, Milton, and Tartaglino, Francis J.: An institutional program for committed sex deviants. *Am. J. Psychiat.* 107:190, 1950.
- ³ Cushing, J. G. N.: Psychopathology of sexual delinquency. *J. Clin. Psychopath.* 11:49, 1950.
- ⁴ Gray, Kenneth G.: Psychiatric evidence in criminal cases. *Am. J. Psychiat.* 106:497, 1950.
- ⁵ Guttmacher, Manfred S.: Adult court psychiatric clinics. *Am. J. Psychiat.* 106:881, 1950.
- ⁶ Haines, William H.: Psychiatrist in court. *Dis. Nerv. System.* 11:273, 1950.
- ⁷ Hawke, C. C.: Castration and sex crimes. *Am. J. Ment. Deficiency.* 55:220, 1950.
- ⁸ Henderson, D. K.: Reflections on criminal conduct and its treatment. *Brit. M. J.* 2:311, 1950.
- ⁹ Kahn, Eugen: Thoughts on problem of psychopathy. *Monatschr. f. Psychiat. u. Neurol.* 118:242, 1949. Abstracted in *Year Book of Neurology and Psychiatry for 1950*. Chicago, Year Book Publishers, Inc., 1950, p. 278.
- ¹⁰ Karpman, B. et al.: The psychopathic delinquent child—Roundtable. *Am. J. Orthopsychiat.* 20:223, 1950.
- ¹¹ McDermaid, Gladys and Winkler, Emil G.: Psychiatric study of homicide cases. *J. Clin. Psychopath.* 11:93, 1950.
- ¹² Overholser, Winfred: Review of psychiatric progress—1949. *Am. J. Psychiat.* 106:541, 1950.

- ¹³ Patterson, Ralph M.: Psychiatric treatment of institutionalized delinquent girls. *Dis. Nerv. System.* 11:227, 1950.
- ¹⁴ Reichard, Suzanne and Tillman, Carl: Murder and suicide as defenses against schizophrenic psychosis. *J. Clin. Psychopath.* 11:149, 1950.
- ¹⁵ Schmideberg, Melitta: On recidivism. *Am. J. Psychotherapy.* 4:286, 1950.
- ¹⁶ Silverman, Daniel: Implications of electroencephalographic abnormalities in psychopathic personality. *Arch. Neurol. & Psychiat.* 62:870, 1949.
- ¹⁷ Williams, J. N.: The individual in confinement. *U. S. Armed Forces M. J.* 1:687, 1950.

Child Psychiatry

By RALPH D. RABINOVITCH, M.D. AND SARA DUBO, M.D.

THE literature in child psychiatry for the year 1951 has been both reiterative and original. The general trends of interest pursue those of the past few years. There is a continuing and growing expression of need for basic research to validate or revise present theories of personality structure and for more such research reports.

Some of the most significant studies have been in the area of direct observation of infants and young children and, stemming from the earlier clarification of the psychogenesis of psychopathic reactions in children, there is widespread concern with the more subtle effects of particular aspects of deprivation in infancy. In the area of theory the stress continues on ego psychology and the *positive* dynamic aspects of the growing personality with an emphasis on experiential rather than instinctual bases for patterns of personality growth. In the clinical field there has been wide interest in childhood schizophrenia, an interest that is proving increasingly productive. In the area of therapy with children this year's literature presents an oft-repeated plea for simplification of concepts and for frank evaluation of technics and results.

In the field in general there are many notes of troubled introspection and discouragement with admonitions that we come from behind the shadowy protection of the symbol to assess the real issues at hand. But pessimism is the inevitable trend of the times, and this is particularly apparent in the attitudes of social scientists. Constructive motivation is dampened by tension and fear. Against this background the literature of 1951 is pervaded by statements of anxiety and concern about the world for our children.

THEORETIC FORMULATIONS

That the field of psychoanalysis is turning increasingly to basic research is evident in many reports in the literature of the past year; that there is movement in the field is also evident in the many shades of opinion and revisions of older theories suggested. A definitive point of view is expressed by Anna Freud²¹ in a major contribution on direct observation of infants and children over a five-year period at the Hampstead Nurseries in Eng-

land; this material was presented by Freud during her recent visit to America.

Direct observation illustrated, confirmed, amended and widened existent analytic knowledge of the phases of pregenital development. One of the most impressive observations was the wide overlapping between oral and anal stages; the line of demarcation between anal and phallic interests seemed in comparison to be much sharper. A further observation relates to the fusion of life and death instincts, or the libido and aggressive energy. From the study of deprived infants who demonstrated inordinate destructiveness Freud postulates that "owing to the stunting of their emotional development, their libido was weaker so that fusion between the drives could not take place in the normal manner." With appropriate stimulation aggression became bound, and "it proved possible, as it were, to effect therapeutic results by bringing about fusion of the two drives."

Freud suggests a number of discrepancies between analytic assumptions based on reconstructions and the findings of direct observation of behavior. In the children observed regression was much more total than analysis has tended to indicate. In addition there tends to be a later telescoping of earlier events; "an action which we see the infant repeat a hundred times may in later life be represented as one traumatic happening." Telescoping was marked in the area of autoerotic activities. Rocking, thumb sucking and rhythmic skin rubbing tend to be overshadowed by later memories of masturbation only. Freud takes note of the fact, however, that these pre-phallic activities may have been unusually prominent in the children observed because of their deprivation and lack of attachment. Observing coitus play without apparent knowledge of the primal scene and oedipal reactions without oedipal experiences, Freud reaffirms her view that "there exist in the child innate, preformed, attitudes which are not originated, merely stimulated and developed by life experience." Of interest to the study of psychopathic children is Freud's final question as to whether "the social reactions learned in a group remain mere ego attitudes or whether they are incorporated into the structure of the personality to form part of the superego, which, according to our present knowledge is built up on the basis of the emotional ties to the parents and the identifications which result from them."

Another point of view, based on psychoanalytic practice and research, is expressed by Johnson.³⁰ In a provocative and stimulating paper she raises some vital questions regarding the relative roles of instinctual forces and experiential forces in character development. She feels that many theoretic emphases of the present must be challenged on the basis of the observations of collaborative psychiatric therapists and the anthropologists. She sees a need to review the entire complex of early development and elaborates on

the following three specific aspects:

1. *Repression as a dynamic mechanism in psychic development.* The view that repression is a primary biologic adaptive mechanism to phylogenetic influences is questioned with this formulation developed: "In the ontogenesis of the individual this adaptive capacity for repression is activated usually by external environmental factors." Johnson, along with Hendrick, points out the pitfalls of adult projection when we consider childhood psychosexual development. She states: "There is no compelling reason to think that the child has a strong impulse to walk or talk at three months. Yet, such an assumption is as defensible as the assumption that the child has a powerful impulse for intercourse at four years." She reiterates Hartmann and Kris' earlier statement criticizing the concept of the phylogenetic source of castration fear, pointing out that "implicit attitudes and anxiety in significant adults are sufficient to cause an intense fear in the child." Referring to anthropologic data, Johnson indicates that character formation does not depend on isolated practices but rather the attitudes with which practices are carried out. Thus: "Early toilet training is compatible with serenity in the child depending upon the mother's attitudes. The view that early interruption of analerotic pleasures regardless of the mother's attitudes must lead to tragedy remains to be demonstrated."

2. *The meaning of restitutive behavior in the child.* Johnson suggests the term 'primary needed object' as more accurate to describe the mother's role with the infant than the traditional term 'primary love object.' She summarizes her views on identification and restitutive behavior as follows: "We cannot understand the formation of the ego and restitutive behavior in many children in terms of guilt toward a love object with subsequent repression of forbidden impulses. . . . Rather, the child makes restitution because it fears the needed object will not fulfil its needs."

3. *The genesis of hostility.* Johnson, like many others in recent years, draws a sharp distinction between aggression and hostile aggression and feels that hostility should be regarded as introjected rather than phylogenetic in origin, in the same way that we regard love as introjected. She develops the theme that hostility finds its origin in the course of the infant's incorporation of the total maternal attitude.

Kris³⁴ continues his attempts, always so productive, to integrate direct observation and reconstructions, in the present paper through a study of early autoerotic activities. He points out that "our views on chronology in zonal sexuality are rapidly shifting. . . . Any attempt to look at the manifestations of zonal behavior in isolation is bound to prove disappointing." Autoerotic self stimulation is seen to arise in part as a substitute for stimulation by the mother. But Kris points out that periodic shifts and reversals of investment between self and object caused by deprivation constitute a

necessary element in normal development, first in differentiating the self from the environment, then in a variety of steps by which the bridge between self and the human object is established by identification. He examines the relationship between rhythmic movement and autoeroticty pointing out that all manifestations of rhythm in a child's life cannot be linked meaningfully to autoeroticty. There are some interesting references to schizophrenic children with the suggestion that autoerotic activity may represent an impediment to normal development.

Hendrick²⁸ speculates as to the processes of early infancy identification mechanisms and relates defects in early identifications to later ego disturbances, which he refers to as "ego defect neuroses." He defines an important differentiation between such neuroses and the more commonly understood neurotic patterns; in the latter, symptoms can be viewed as defense functions of the ego serving for the avoidance of anxiety; in the ego defect neuroses the symptoms result from a fundamental inadequacy of some essential functions of the ego itself.

The effects of deprivation in infancy have received increasing attention in recent years and there has been wide application of observations in this area to basic research in personality development, especially problems of identification and pregenital sexuality. This past year has seen even wider expansion of this interest. Bowlby,⁹ in a World Health Organization monograph, provides an outstanding synthesis of present knowledge regarding the effects of early deprivation. His survey indicates that numerous direct, retrospective and follow-up studies arrive at remarkably similar views regarding the destructive influence of prolonged early deprivation on capacity for later superego awareness and social identification. Beyond this documentation of research, Bowlby discusses convincingly the validity of early adoption, preferably in the first few months of the infant's life, and reviews the general problem of foster home and institutional care for neglected children. This monograph represents essential reading for all workers in the children's field.

Levy,³⁷ in a theoretic discussion of the genesis of psychopathic reactions in children, differentiates between the deprived psychopath and the indulged psychopath. Differentiating the two etiologic groups Levy points out that "the deprived psychopath is presumably unable to adjust to life because of his inability to form a close human relationship; . . . in the indulged psychopath the superego is weak because the identification is so strongly represented by the indulgent loving mother. The deprived psychopath is defective in the capacity to develop 'standards.' In the indulged psychopath, standards are well understood, but taken lightly." Attempting to refine understanding of specific distortions in the primary mother relationship Rabinovitch⁴⁹ expresses the view that such studies "may allow us

ultimately to broaden the concept of constitution beyond predestination and anthropometric levels to an understanding of basic individual differences in primary needs that can be met through preventive efforts." In place of the term psychopathic personality, which he feels is often used as "a meaningless opprobrium with constitutional insinuations," Rabinovitch suggests the term 'primary psychogenic acathexis'; "this would seem to describe the child's basic problem, his inability to invest relationships and thoughts with feeling and significance. It also points to the usual psychogenesis, disturbance in the primary mother cathexis."

While we can recognize in the literature broad agreement as to the effects of early deprivation, the question of therapy in such cases is by no means as clear. Freud and Dann²² report an interesting study of six early-deprived children observed in residential treatment. While these children showed limited relationship capacity with adults they exhibited a very close group identification. Considering the atmosphere of tension and fear in which they had grown, much less anxiety was found than might have been expected and the authors conclude that it remains an unanswered question as to why their experiences had not predisposed them to more violent anxiety states. Bennett and Hellman⁵ report on the direct observation of one child, separated early from his mother, and later, some years after the direct observations were recorded, treated analytically. While in this first study they come to no definitive conclusions, the combination of early observation and later analysis would seem to hold great promise as a research method.

Spitz⁵⁵ attempts what he calls a "preliminary" and "crude" etiologic classification of the psychogenic diseases in infancy. In these disturbances, Spitz considers the mother's personality to act as a disease-provoking agent, a psychologic toxin, and he refers to a group of conditions as the "psychotoxic diseases of infancy." Attempting to relate specific diseases to specific etiologic factors in the maternal attitude, he suggests the following: coma in the newborn is equated with overt primal rejection; three-month colic with primary anxious overpermissiveness; infantile neurodermatitis with hostility in the garb of anxiety; hypermotility (rocking) with oscillating between pampering and hostility; fecal play with cyclical mood swings; aggressive hyperthymic with hostility consciously compensated. In addition to these psychotoxic diseases Spitz refers to two deficiency diseases of infancy, anaclitic depression which he correlates with partial emotional deprivation and marasmus equated with complete functional deprivation.

CLINICAL STUDIES

The principles of developmental psychology are being gradually integrated in numerous pediatric and educational settings. In the past year a

number of books illustrating these applications have appeared. Gesell²⁴ provides a compact orientational volume which interprets the pattern of prenatal and infant behavior illustrated by action photographs. Writing with the special needs of teachers in mind, "the largest single professional group working with children," Olson⁴⁴ provides a most valuable detailed report of comprehensive research in child development carried out in a laboratory school. Mead and Macgregor,⁴² analyzing a large number of photographs of a small group of Balinese children and their parents, and comparing these with data on American children, attempt to survey some problems of the interrelationships between growth and culture. Watson and Lowrey⁵⁸ have written a small but inclusive volume on growth and development directed particularly to the interests of the pediatrician.

A major contribution to the year's literature is a book on child psychiatric technics by Bender.² This is a collection of papers by Bender, Schilder and a number of collaborators and represents a portion of the voluminous research data that have come from the Children's Service of the Psychiatric Division at Bellevue Hospital. These papers are concerned for the most part with projective, creative and configurational studies and applications in therapy, and with the group behavior of disturbed children. New material on children's art is particularly noteworthy. The book contains a wealth of original insights with wide clinical applicability and represents a unique contribution to the children's field. It is the first of a series of three volumes by Bender. Studies on the psychopathology of childhood and on clinical psychiatric syndromes in childhood are to follow.

A critical survey of existing concepts regarding psychopathic behavior in infants and children has been compiled by Karpman. Six contributors discuss the topic from varied points of view. The papers of Levy³⁷ and Rabinovitch⁴⁹ have been referred to earlier in this chapter. Lurie⁴¹ attempts to equate psychopathic behavior in children with brain injury and poses the question: "May not this inability to relate be due to the presence of unrecognized and irremediable organic pathologic factors?" Lippman³⁸ describes the extreme narcissism and the instinct-driven quality of the behavior of dissocial children, and he points to the difficulties in their treatment. The goal of therapy is to change the narcissistic tie to an object transference relationship which would eventually lead to superego development, and Lippman speculates interestingly as to methods for achieving this goal. Lowrey⁴⁰ deplores the indiscriminate overusage of the term constitution as an essential immutable factor as applied to the etiology of psychopathic reactions. He writes: "The only type of psychopathic reaction which needs so far to be definitely delineated in the preschool years is the one that is dependent upon isolation and affect hunger for which the symptom picture and prognosis are fairly well established." The late Doctor

Lucien Bovet,⁸ who met an untimely accidental death during the past year, prepared a valuable report on psychiatric aspects of juvenile delinquency, studied in a number of European countries and America; his monograph, prepared on behalf of the World Health Organization, presents a thoughtful synthesis with many valid recommendations for progress.

The growing attention to problems of the brain-injured child, apparent in the recent literature, represents a research interest both essential and long overdue. In a highly rewarding, inclusive, yet concise paper Bender³ gives further attention to the psychologic problems and specific treatment needs of the encephalopathic child. Factors influencing the adaptation of organically handicapped children are considered by Chess and Carter.¹¹ In studies of 24 handicapped children the authors conclude that the most common symptom is anxiety about attempting new experiences or facing new situations. Parental attitudes have profound influence on the child's courage and readiness to deal realistically with life situations. Bonnard,⁷ drawing upon her experiences in a child guidance clinic in London during the last War, provides an interesting clinical study of the consequences of war injuries, real and imaginary, in children. Rather than the air raids and ensuing shock episodes themselves, the major traumatic factor in the situation was the fright and panic manifested by parents or parent substitutes. This report contains some excellent case illustrations.

Problems of speech comprehension are considered in a collection of papers in an issue of the "Nervous Child"²⁷; the symposium contains a number of valuable contributions with special attention devoted to problems of deaf and aphasic children. In a consideration of diagnostic evaluations of children with expressive handicaps, Doll¹⁵ raises the pertinent issue of the unreliability of most psychometric tests for such children. Generally the tests assume sensory integrity, motor integrity and absence of emotional interference and, in children with expressive handicaps, these factors may be impaired. The etiology of reading disabilities in children remains an open field for speculation. Fabian¹⁷ attempts a compromise solution of the problem in his report on clinical and experimental studies of 20 children showing retarded reading.

Summarizing his conclusions he states: "A learning disability is one of many symptoms which the ego-disabled, emotionally retarded, infantile, dependent children show." Bender and Schilder,⁴ in an earlier study of reading disability reported this year, conclude that "the difficulty appears to be due to a lag in development of the specific functional patterning in the parietal and occipital areas of the brain." Personality problems and neurotic reactions are recognized; these are considered to be secondary and basically unrelated etiologically to the reading disorders. In a further study on the use of the draw-a-family technic in diagnostic interviews, Hulse²⁹ provides

14 case summaries with some fascinating drawings of the family included; the material gives graphic illustration of a valuable technic and Hulse's interpretations are most helpful.

In the field of mental deficiency, Sarason⁵⁵ contributes a volume of major importance. He brings together in a book a comprehensive review, with searching critical analyses of significant research data, and documents with numerous extensive quotes much of the significant literature in the field. His study, with many case illustrations, can be considered a source book on present theory and practice in the field. Genetic factors in deficiency are given detailed consideration in a text from England by Penrose⁴⁵ on the biology of mental defect.

Several noteworthy studies have appeared on the problem of sexual disturbance in children and adolescents. Etiologic factors are reviewed and a research approach along with plans for preventive and therapeutic measures are outlined in a multi-discipline Commission Report from the State of Michigan.⁵⁶ Continuing his studies of children's sex awareness and sex attitudes, Conn¹² reports an investigation into the appreciation of sex differences revealed by children through their play patterns and game preferences. Fraiberg²⁰ considers the manner in which children may integrate sexual knowledge given them by parents or therapists. Often what the adult means to prove enlightening leads to confusion, because the child distorts the material to fit in with his own theories that serve his neurosis in some way.

In the past year there have been relatively few psychosomatic studies relating to children. Prugh⁴⁷ has investigated the role of emotional factors in idiopathic celiac disease. Intensive multi-discipline studies were carried out in 14 cases. Findings indicate physiologic disturbances with autonomic and adrenal cortical involvement, a genetic factor, and distortion in the mother-child relationship. No single etiologic factor was found operative; emotional factors, however, may serve as a trigger mechanism. Potentialities for the application of group therapy in pediatric hospital practice are discussed by Dubo.¹⁶ Her paper stresses the importance of viewing hospitalization as a social experience for the child, and outlines methods through which relationships and group contacts may be used optimally in the total treatment program. Illustrations from interview group therapy with tuberculous and allergic children are included.

CHILDHOOD SCHIZOPHRENIA

The year's literature on childhood schizophrenia is particularly extensive and we can refer to only a few representative studies. Kanner³¹ adds further to his description of the psychopathology of early infantile autism stressing the importance of maintaining the status quo in the life of the young

schizophrenic child. There is intense resistance to change and only the child himself may modify existing conditions. His behavior differs from ordinary obsessive ritualism in a significant respect—the autistic child forces the people in his world to be even more obsessive than he is himself. The question of etiology in childhood schizophrenia remains open and challenging; several authors this year suggest etiologic formulations. Despert¹⁴ describes one case in detail in an attempt to clarify the relation of maternal behavior to the development of an autistic pattern in a young child. She raises the question as to whether very early distortions in the mother-infant relationship may not lead to the core problem of disturbance of contact with reality, which she feels may be noted in some cases during the first months of life. In another detailed single case study of major interest, Putnam, Rank and Kaplan⁴⁸ equate childhood schizophrenia with primal depression of infancy. The chronic depression preceding severe regression is caused by marked ambivalence on the part of the mother with resultant repeated disappointments for the child. An interesting longitudinal study covering 28 years in the life of a girl, diagnosed at the age of four as a case of early infantile autism, is presented by Darr and Worden;¹³ when studied at the age of 32 she presented a typical adult schizophrenic picture. Treatment of a schizophrenic child in a child guidance clinic is reviewed with many positive insights by Fabian and Holden.¹⁸ Gurevitz²⁶ speculates as to the applicability of direct analytic therapy (Rosen) and the technic of symbolic realization (Sechehaye) in the treatment of schizophrenic children. In a well-documented study, Bergman, Waller and Marchand⁶ report on schizophrenic children found in the population of a State school for mental defectives.

THERAPY

Dr. Richard C. Cabot in his 1931 Presidential address to the National Conference of Social Work advised the group to "measure, evaluate, estimate, appraise your results in some form in any terms that rest on something beyond faith, assertions and illustrative cases." Putting into practice this admonition, Dr. Cabot launched in 1937 the monumental Cambridge-Somerville Youth Study, designed to test the value of long-term guidance in the prevention of delinquency. Two groups of 350 boys each were matched; one group (the T group) received counselling, the other group (the C group) received no organized special help. The project continued over a period of some seven years and detailed reports of the experimental design and the results are reported in a book by Powers and Witmer.⁴⁶ Throughout the project 19 counsellors worked with the T boys; eight were professional social workers, six had completed part training in social work, two were group workers, two were psychologists and one a trained nurse.

At the time treatment began the majority of the boys were past the age of 10 with the largest group being 11 and 12. The therapeutic contacts were for the most part unstructured and often informal and by design the therapist's role was that of a "friendly counsellor." In terms of police department records results indicate that the special work of the counsellors was no more effective than the usual forces in the community in preventing boys from committing delinquent acts. The first half of the book consists of a general review of the project by Powers; in the second half Witmer, "an outsider," attempts an objective qualitative study and evaluation of the entire project. Her careful analyses of individual cases represents an important clinical contribution to the field of delinquency. It is interesting to note that the most successful counsellor was the nurse and Witmer analyzes the factors contributing to her success. While the results of this long-term counselling are very discouraging the project itself represents an important milestone in our field; for the first time a forthright and detailed large-scale research evaluation of the results of therapy has been completed. That a similar design be applied to other therapeutic approaches seems imperative. At this point we cannot compare the results of this counselling with those of more orthodox therapies because we have no analagous evaluations to go by. We would hope that results would be more favorable but there is one small item in Witmer's report that suggests an urgent need for this type of courageous study; Witmer tells us that of a group of control cases who became clients of psychiatric clinics or social agencies in no case was treatment at all successful. Details are lacking and no conclusions can be drawn but the need for serious evaluative studies is clearly demonstrated.

Many of the year's papers on psychotherapy with children stress the need for deritualizing some of our technics and simplifying concepts. Thus, Rexford quotes Rank⁵¹ as pointing out the value in psychotherapy with children of "concentrating upon the area of immediate conflict without a foray into other possible difficulties unless necessary." Burlingham¹⁰ questions the validity in many cases of the traditional clinic practice of providing different therapists for child and mother expressing the view that if the therapist does not have direct and sustained contact with the mother the analysis of the child may be doomed to failure. Fraiberg,¹⁹ discussing the application of psychoanalytic principles in casework practice with children, notes that each child presents different needs in therapy and that she is "not concerned about the problem of whether social workers should be doing deep therapy or superficial casework, whatever these differences may be, but that there be deep thinking, not superficial thinking in every phase of casework practice. Through case studies she shows how "deep thinking" may indicate the need for "superficial therapy."

Ginsburg²⁵ raises the question of how objective the therapist can or should

be and points out that "consciously or otherwise we help people to be like ourselves." Complete objectivity, while the purported goal of psychoanalytic therapy, according to Ginsburg, is unattainable and "a goal that would not necessarily be desirable were it possible." Schmideberg⁵⁴ gives similar stress to the need for spontaneity especially in casework with children. She warns against over-theorizing and over-resorting to the psychiatric cliché, advising that "we must check carefully in every case whether the facts bear out the theory." With accustomed directness she states: "Psychoanalytic theory is useful for a better understanding of situations and in handling the client, so long as it does not interfere with the spontaneous human attitude."

There is somewhat less material than usual this year on residential treatment of disturbed children but a major contribution is a volume by Redl and Wineman⁵² on the disorganization and breakdown of behavior controls in disturbed boys studied in a small residential treatment unit. There is an elaborate analysis of ego deficiencies with a listing of 22 ego functions that may be impaired in the poorly functioning delinquent child. Rabinovitch, Bee and Outwater⁵⁰ describe the organization of a psychiatric treatment service in a university hospital setting and define in detail with case material the integration of occupational and recreational therapy in the total treatment program. Alt¹ explores the responsibilities of various disciplines in a functioning residential treatment unit and presents a valuable synthesis of the problem.

THE GENERAL FIELD

Further encouraging opportunities for international discussion of children's problems have been provided this past year. The Annual Report for 1950 of the World Federation for Mental Health⁵⁰ exemplifies the feasibility of group discussion and interdisciplinary exchange in planning for children on a broad level. Many topics pertinent to the field of child psychiatry were considered at the Fourth International Congress on Mental Health held in Mexico City in December 1951. More than 800 delegates, representing 37 countries, attended the Congress; the published proceedings should be available by the Fall of 1952. Some disquieting comments on the relationship between the American culture and emotional illness were voiced. Fromm,²³ in a brilliant paper, outlines obstacles to comfortable growth that the culture imposes: "Our contemporary Western society . . . is increasingly less conducive to mental health; man has become a commodity . . . developing the kind of personality which is in demand on the personality market. He has to have the feeling and ideas which are not contrary to anyone, he has to develop a 'pleasant personality' whose *opinions* are always up to date and who has no *convictions* and no doubts." Kirkpatrick,³³ at the same

Congress, points to the status-mindedness of our culture and the problems that this raises for adolescents: "Families quite generally fail to expect the maximum satisfaction from the present because the present is being sacrificed for the prospects of future gain."

There are many other pertinent comments on the American scene as it affects our work with children. Montagu⁴³ reviews the evidence for a positive innate drive toward growth and normality and examines cultural pressures that produce frustrations and distortions of the normal drive. LaBarre³⁵ offers some reassuring thoughts regarding the permanency of the American family but in the course of reassurance a jeremiad, expressed so often today, intrudes: "We shall have the family so long as human beings are around and our major concern is literally whether or not there will be human beings around." Towle⁵⁷ examines problems of contemporary family security with unusual clarity and vision and raises an issue vital to all workers in the mental health field. Referring to the importance of social participation by group workers Towle writes: "Work of this nature is impeded in times when every organized group is suspect, when freedom of speech is curtailed, and when actions to make one's views known endangers the standing of loyal citizens."

The use of psychiatric concepts in parent education and the influence of psychologic insight on the spontaneity of mothers are topics of growing concern to the field. Mead⁴² examines and deplores the cultural factors that have led to the misapplication by parents in America of Gesell's original developmental concepts. Kanner³² outlines three major cultural forces that have contributed to the dilemma of today's mother: her work before marriage, mechanization in pediatric practices and intimidation of mothers by psychologists and psychiatrists. He points out that "mothers need less universal censure, less wholesale condemnation and more sympathetic understanding." Lourie³⁹ voices concern about the translation of psychiatric concepts into pediatric practice. He recognizes the validity of optimal gratification for infants but points out, reflecting a growing point of view: "We may have oversold ourselves with certain people. We have to be around to set matters right when we have sold self-demand feeding, for example, to an insecure, dependent or obsessional mother. We have to be ready to handle the guilt we have created in the conscientious mother who is unable for any reason to breast-feed her baby. We have to stop some of our company from becoming too rigid about being liberal."

Finally, we should like to refer to a contribution of major importance by Levy,³⁶ his 1951 Academic Lecture before the American Psychiatric Association, in which he presented a critical evaluation of the present state of child psychiatry. In a stimulating and provocative talk, Levy reviews the historical background of child psychiatry in America and raises some

vital issues facing the field today. He elaborates on the difficulties of integration of the psychiatric, psychological and social service disciplines in actual practice, deploring the lack of clarity of function of the three groups. Levy stresses the importance of diagnosis as a prerequisite to any planning or treatment for children and views with alarm "an antidiagnostic attitude" prevalent in some clinics. The emphasis is on the importance of a medical orientation in child psychiatry, "respecting the art of medicine as primarily a therapeutic function, involved, therefore, of necessity with diagnostic and prognostic study." Levy makes pointed reference to some weaknesses in the orientation of both child guidance and child psychiatry pointing especially to tendencies toward diffusion or narrowness. He offers challenging suggestions for the future and predicts a closer affiliation of child psychiatry with the hospital and medical clinic.

REFERENCES

- ¹ Alt, H.: The role of the psychiatric social worker in the residential treatment of children. *Social Casework*. 32:363, 1951.
- ² Bender, L.: *Child Psychiatric Techniques*. Springfield, Ill., Charles C Thomas, 1951.
- ³ —: The psychological treatment of the brain damaged child. *Quart. J. Child Behav.* 3:123, 1951.
- ⁴ — and Schilder, P.: Graphic art as a special ability in children with a reading disability. *J. Clin. & Exper. Psychopath.* 12:147, 1951.
- ⁵ Bennett, I. and Hellman, I.: Psychoanalytic material related to observations in early development. *In The Psychoanalytic Study of the Child*. New York, The International Universities Press, 6, p. 307.
- ⁶ Bergman, H., Waller, H., and Marchand, J.: Schizophrenic reactions during childhood in mental defectives. *Psychiatric Quart.* 25:294, 1951.
- ⁷ Bonnard, A.: Some examples and consequences of war injury, real and imaginary, in children. *Quart. J. Child Behav.* 3:1, 1951.
- ⁸ Bovet, L.: *Psychiatric Aspects of Juvenile Delinquency*. World Health Organization Monograph, Series No. 1, World Health Organization, Geneva, 1951. (New York, Columbia University Press.)
- ⁹ Bowlby, John: *Maternal Care and Mental Health*. World Health Organization Monograph, Series No. 2, World Health Organization, Geneva, 1951. (New York, Columbia University Press.)
- ¹⁰ Burlingham, D. T.: Present trends in handling the mother-child relationship during the therapeutic process. *In The Psychoanalytic Study of the Child*. New York, The International Universities Press, 1951. 6, p. 31.
- ¹¹ Chess, S. and Carter, V. E.: Factors influencing the adaptation of organically handicapped children. *Am. J. Orthopsychiat.* 21:827, 1951.
- ¹² Conn, J. N.: Children's awareness of sex differences. *J. Child Psychiat.* 2:82, 1951.
- ¹³ Darr, G. C. and Worden, F. G.: Case report twenty-eight years after an infantile autistic disorder. *Am. J. Orthopsychiat.* 21:559, 1951.
- ¹⁴ Despert, J. L.: Some considerations relating to the genesis of autistic behavior in children. *Am. J. Orthopsychiat.* 21:335, 1951.

- ¹⁵ Doll, E. A.: Mental evaluation of children with expressive handicaps. *Am. J. Orthopsychiat.* 21:148, 1951.
- ¹⁶ Dubo, S.: Opportunities for group therapy in a pediatric service. *Internat. J. Group Psychotherapy.* 1:235, 1951.
- ¹⁷ Fabian, A. A.: Clinical and experimental studies of school children who are retarded in reading. *Quart. J. Child Behav.* 3:1, 1951.
- ¹⁸ — and Holden, M. A.: Treatment of childhood schizophrenia in a child guidance clinic. *Am. J. Orthopsychiat.* 21:571, 1951.
- ¹⁹ Fraiberg, S. H.: Applications of psychoanalytic principles in casework practice with children. *Quart. J. Child Behav.* 3:175; 250, 1951.
- ²⁰ —: Enlightenment and confusion. *In The Psychoanalytic Study of The Child.* New York, The International Universities Press, 6, p. 325.
- ²¹ Freud, A.: Observations on child development. *In The Psychoanalytic Study of the Child.* New York, The International Universities Press, 1951, 6, p. 18.
- ²² — and Dann, S.: An experiment in group upbringing. *In The Psychoanalytic Study of the Child.* New York, The International Universities Press, 1951, 6, p. 127.
- ²³ Fromm, E.: The contribution of the social sciences to mental hygiene. Paper read at the Fourth International Congress on Mental Health, Mexico City, Dec., 1951.
- ²⁴ Gesell, A.: *Infant Development. The Embryology of Early Human Behavior.* New York, Harper & Brothers, 1951.
- ²⁵ Ginsburg, S. W.: The impact of the social worker's cultural structure on social therapy. *Social Casework.* 32:319, 1951.
- ²⁶ Gurevitz, S.: Direct analytic therapy and symbolical fulfilment—reviewed as to their applicability in childhood schizophrenia. *Quart. J. Child Behav.* 3:276, 1951.
- ²⁷ Harms, E. (ed): Problems of speech comprehension. *Nerv. Child.* 9: No. 1, 1951.
- ²⁸ Hendrick, I.: Early development of the ego: identification in infancy. *Psychoanalyt. Quart.* 20:44, 1951.
- ²⁹ Hulse, W. C.: The emotionally disturbed child draws his family. *Quart. J. Child Behav.* 3:152, 1951.
- ³⁰ Johnson, A., McF.: Some etiological aspects of repression, guilt and hostility. *Psychoanalyt. Quart.* 20:511, 1951.
- ³¹ Kanner, L.: The conception of wholes and parts in early infantile autism. *Am. J. Psychiat.* 108:23, 1951.
- ³² —: Emotional and cultural impacts on contemporary motherhood. *J. Child Psychiat.* 2:168, 1951.
- ³³ Kirkpatrick, M. E.: The mental hygiene of adolescence in the Anglo-American culture. Paper read at the Fourth International Congress on Mental Health, Mexico City, Dec., 1951.
- ³⁴ Kris, E.: Some comments and observations on early autoerotic activities. *In The Psychoanalytic Study of The Child.* New York, The International Universities Press, 1951, 6, p. 95.
- ³⁵ LaBarre, W.: Appraising today's pressures on family living. *Social Casework.* 32:51, 1951.
- ³⁶ Levy, D. M.: Critical evaluation of the present state of child psychiatry. *Am. J. Psychiat.* 108:481, 1951.
- ³⁷ —: The deprived and the indulged forms of psychopathic personality. *Am. J. Orthopsychiat.* 21:250, 1951.

- ³⁸ Lippman, H. S.: Psychopathic reactions in children. *Am. J. Orthopsychiat.* 21:227, 1951.
- ³⁹ Lourie, R. S.: Psychopathic behavior in infants and children—the pediatric-psychiatric viewpoint. *Am. J. Orthopsychiat.* 21:237, 1951.
- ⁴⁰ Lowrey, L. G.: The development of psychopathic reactions. *Am. J. Orthopsychiat.* 21:242, 1951.
- ⁴¹ Lurie, L. A.: Psychopathic behavior of little known or idiopathic origin. *Am. J. Orthopsychiat.* 21:224, 1951.
- ⁴² Mead, M. and Macgregor, F. C.: *Growth and Culture; a Photographic Study of Balinese Childhood.* New York, G. P. Putnam's Sons, 1951.
- ⁴³ Montagu, A.: *On Being Human.* New York, Henry Schuman, 1951.
- ⁴⁴ Olson, W. C.: *Child Development.* Boston, D. C. Heath, 1949.
- ⁴⁵ Penrose, L. S.: *The Biology of Mental Defect.* New York, Grune & Stratton, 1949.
- ⁴⁶ Powers, E. and Witmer, H.: *An Experiment in the Prevention of Delinquency; the Cambridge-Somerville Youth Study.* New York, Columbia University Press, 1951.
- ⁴⁷ Prugh, Dane G.: A preliminary report on the role of emotional factors in idiopathic celiac disease. *Psychosom. Med.* 13:220, 1951.
- ⁴⁸ Putnam, M. C., Rank, B. and Kaplan, S.: Notes on John I.: A case of primal depression in an infant. *In The Psychoanalytic Study of the Child.* New York, The International Universities Press, 1951, 6, p. 38.
- ⁴⁹ Rabinovitch, R. D.: The concept of primary psychogenic acathexis. *Am. J. Orthopsychiat.* 21:231, 1951.
- ⁵⁰ —, Bee, J., and Outwater, B.: The integration of occupational and recreational therapy in the residential psychiatric treatment of children; a symposium. *Am. J. Occup. Therapy.* 5:1, 1951.
- ⁵¹ Rank, B. and Kaplan, S.: A case of pseudoschizophrenia in a child—Workshop, 1950. *Am. J. Orthopsychiat.* 21:155, 1951.
- ⁵² Redl, F. and Wineman, D.: *Children Who Hate; The Disorganization and Breakdown of Behavior Controls.* Glencoe, Ill., The Free Press, 1951.
- ⁵³ Sarason, S. B.: *Psychological Problems in Mental Deficiency.* New York, Harper & Brothers, 1949.
- ⁵⁴ Schmideberg, M.: Psychiatric-social factors in young unmarried mothers. *Social Casework.* 32:3, 1951.
- ⁵⁵ Spitz, R. A.: The psychogenic diseases in infancy; an attempt at their etiologic classification. *In The Psychoanalytic Study of the Child.* New York, The International Universities Press, 6, p. 255.
- ⁵⁶ State of Michigan: Report of the Governor's Study Commission on the Deviated Criminal Sex Offender. Lansing, 1951.
- ⁵⁷ Towle, C.: Reinforcing family security today. *Social Casework.* 32:57, 1951.
- ⁵⁸ Watson, E. H. and Lowrey, G. H.: *Growth and Development of Children.* Chicago, The Year Book Publishers, 1951.
- ⁵⁹ World Federation for Mental Health: *Annual Report for 1950.* London, 1951.

The Neuroses

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GENERAL CONSIDERATIONS

DURING the past year, lay interest in the neuroses and personality disorders continued intense, as indicated by the frequency of these themes in television and movie scripts, syndicated newspaper columns and cartoons such as those of Gould²¹ or Wiggam⁵⁵ and the flood of articles on pastoral and other counselling by Boisen,⁶ Weigert⁵⁴ and others. Similarly, the public continued to be avid for individualistic and over-simplified books written by non-psychiatrically trained medical men such as Alvarez.³ More authoritatively, Bowman and Rose⁷ advocated the abolition of the timeworn terms *neuroses*, *psychoneuroses*, and *psychoses* because of their ambiguity and misuse; whereas Yap⁵⁹ too, challenged the general validity of our current psychiatric concepts. The latter author emphasized once again that the term "normal" has reference only to the adjustments and adaptations of the individual to his current social milieu; and cited the fact that homosexuality, touch taboos and suicide are considered normal modes of behavior in certain cultures. In this connection, Moloney³⁵ discussed the manner in which allegiances to the Emperor as a father-surrogate influences even psychotic behavior in the Japanese, and, therefore, questions the wisdom or possibility of attempting to impose Western concepts of democracy upon an oriental culture so fundamentally different from our own.

ETIOLOGIC CONSIDERATIONS IN THE NEUROSES

Under this heading, various authors considered the effects of (1) heredity, (2) early environment, (3) traumatic experiences in later life, and (4) combinations of these. The following publications are representative.

Heredity. Zahle⁶⁰ agrees basically with the Kraepelinian view that to a large degree manic-depressive psychosis is hereditarily or constitutionally determined, but concedes that psychogenic elements do exist in this illness as well as in "psychogenic depressions." He recommends psychotherapy for

both conditions but considers electro-shock therapy to be specific for the manic-depressive cycle. Croft¹⁴ observed "neurotic" behavior in cows, horses, dogs, and cats and asserts categorically that these are inherited deviations relatively unaffected by environment.

Early Environment. Bieber⁵ defines pathologic boredom as a repression of creativeness resulting in an incapacity to act in some important area of life; pleasure inhibitions begin early in response to the restrictive demands of parents, society, and reality, whereas work inhibitions result from sibling rivalries and the Oedipus situation. Work and achievement also may be a weapon of competition, in which case sterile perfectionism constitutes a defense against unconscious guilt and anxiety.

Traumata in Later Life. Freeman¹⁶ postulates that men who envy the functions of pregnancy in women may be seriously disturbed by latent impulses of jealousy and hate; when such impulses can no longer find expression in sexual drives, symptom formation becomes necessary to reduce intra-psychic tension. Straker⁵¹ observes that surgical procedures may also release pathologic amounts of anxiety and thus determine the onset of a neurotic illness; he recommends the cultivation of reassuring doctor-patient relationships, adequate sedation, and the judicious use of anaesthesia as preventive procedures. Kamman²⁵ lists three etiologic factors in traumatic neuroses: (a) a narcissistic regression to attitudes of dependence not directly related to financial compensation, (b) unconscious desire for gain, and (c) "attitudinal pathosis," compounded of dependence and hostility, leading to defensive rationalizations and self-justifications.

Sociologic Factors. Henry,²³ in accord with Harry Stack Sullivan's emphasis on deviations in interpersonal relations, defines a neurosis as a relatively rigid pattern of interaction adapted by the individual from early intra-familial attitudes and projected upon the world in such a manner as to engender reciprocal responses from others. Henry urges early and prolonged observation—even to the extent of having a social worker live for a time with the family—as a necessary research technic. The development of personal traits such as dominance, clinging, and provocative behavior could thus be observed, later correlated with other facts from the personal history, and eventually used to validate and expedite treatment.

Geriatric. Clow and Allen¹² report a study of neurotic and psychotic patients sixty years of age or over; in 50 of the 67 cases, environmental stresses were demonstrably important as precipitating factors in their illness.

Combinations of Above. Ripley and Wolf,⁴⁰ after a study of 1800 neuropsychiatric patients in the Southwest Pacific during World War II, report that unfavorable early environment, adverse familial tendencies, and pre-service maladjustments were definite predisposing factors in psychiatric

disorders; nevertheless, they were unable to determine whether or not their subjects would have become ill had they not been exposed to combat stress. Gordon²⁰ and Miles and Cobb³³ likewise conclude that all possible combinations of organic and functional factors may operate in precipitating various psychiatric disorders.

RESEARCH STUDIES

Cohen¹³ compared the palmar perspiration of "normal" hospital attendants with that of "neurasthenic" subjects by weighing pieces of blotting paper before and after application to the palms of each; Cohen observed that whereas the "neurasthenics" showed a higher baseline of palmar sweating, both groups responded equally to stress; on the other hand, organic diseases such as thyrotoxicosis or autonomic nervous system imbalance produced divergences from normal levels greater than those observed in either the control or "neurasthenic" groups. Similarly, Clausen¹¹ was unable to demonstrate statistically valid differences in the type and rate of respiration of normal, neurotic, and psychotic individuals.

Animal Experiments. Masserman et al.,³¹ using direct, square wave and 60-cycle, sine wave currents to induce convulsions in normal and neurotic cats, demonstrated that both "neurotic" and "normal" behavior were disorganized to a degree corresponding with the disintegration of all recently learned complex patterns.

PSYCHOSOMATIC CORRELATIONS*

Subjective Well-Being. Harris²² had the mothers of children brought to his clinic as behavior problems rate themselves as regards good health, fatigability, and headache. Subsequent psychiatric interviews led him to conclude that a feeling of well-being is dependent upon the gratification of basic needs and upon the ability to discharge anger externally when these needs are not satisfied; conversely, feelings of ill health result from frustrations and repressions. Malmö et al.²⁹ also call attention to the tendencies of patients to utilize specific organs or systems to manifest anxiety but offer no explanation as to the nature or dynamics of this specificity.

Neurocirculatory Asthenia. Oppenheimer and Gertler³⁸ and Margolin³⁰ imply that neurocirculatory asthenia is not in itself a clinical entity but merely an exaggeration of the cardiovascular aspects of the symptomatology of anxiety. They urge symptomatic therapy bolstered by the removal of the possibility of secondary gain.

Acne Vulgaris. Wittkower⁵⁶ studied the personalities of 64 adult patients with acne vulgaris and attempted to classify them into definite character types. In Wittkower's opinion, all of his patients were emotionally arrested

* Only papers not reviewed in chapter 29 are here surveyed.

at the stage of puberty, i.e., they denied sexual desires, dreaded marriage, and avoided many normal social obligations—patterns of conduct that might also be interpreted as defenses against feelings of inferiority and isolation.

Colonic Dysfunctions. Seward⁴⁷ reviews the anatomy, physiology, and clinical significance of colonic activity and concludes that "colon neuroses," under which he groups colon consciousness, mucous colitis, and spastic or irritable colon, may be traced to the influence of anxious mothers, who, by wrong feeding or by compelling bowel regularity in their children through enemata and cathartics, led them to utilize patterns of colonic symptomatology as an expression of anxious passivity or hostility throughout life.

Rhinology. Brown⁸ differentiates between sufferers from allergies, infections, polyps, or other physical causes of nasal congestion on the one hand, and "nasal neurotics" on the other; the latter, according to Brown, derive sensory gratification from the passage of cool air over an abnormally shrunken turbinate mucosa and are, therefore, avid users of nasal decongestants or may even demand turbinate resection. Brown suggests the administration of nasal drops of decreasing strength, and combines this medication with reassurance and other psychotherapy.

Surgery. Rosen⁴² advocates clinical circumspection and conservatism in surgery involving resection of any portion of the body. He points out the necessity of learning preoperatively the meaning and valuation ascribed by the patient to the part to be removed and believes that in this way many so-called toxic and postoperative psychoses may be averted by preventive psychotherapy.

MILITARY CONSIDERATIONS

Sherman⁴⁸ reviews some of the lessons of World War II and suggests that previous methods of psychiatric induction screening have been inadequate and wasteful. He believes that too often mild anxiety symptoms were considered sufficient reason for rejection and suggests that a continuous screening system be devised using the inductee's actual performance in service as a basis for selection. Sacks⁴³ reports the experience of the Army Medical Test Team during the winter of 1948-49 in the Arctic; he concludes that there are no personality types that tend to do better than others under the stress of Arctic isolation and confinement, but that satisfactory adjustment is dependent upon emotional stability and a successful record of performance prior to Arctic assignment.

Glass¹⁹ and Zuska⁴⁸ point out that the terms "combat fatigue" or "combat exhaustion" are preferable to "combat neurosis" because the former imply recovery and can not be used as discharge diagnoses. Glass stresses the importance of emotional ties between the soldier and his comrades,

groups, and leaders in preventing combat reactions and comments that persons who are unable to mobilize or externalize aggression or who demonstrate too much or too little conscience are those most likely to break down under military stress.

Ranson,³⁹ in outlining the treatment of psychiatric casualties at different echelons of the Army organization, also emphasizes the desirability for early therapy, based upon the individual's identification with the forward combat group, as a means of minimizing secondary gains and connotations of illness and disability. If evacuation becomes necessary, a single continuous channel should be employed for all neuropsychiatric casualties. At the Battalion Aid Station level, it is advisable to treat as many patients as possible on full duty status; rest and sedation may be employed, but the attitude must be one of sympathetic firmness, and with full expectation that the men will return to combat duty. At the Division Clearing Station and the Army Neuropsychiatric Treatment Station, care is based upon treatment of fatigue and exhaustion, alleviation of deprivations and individual psychotherapy. The latter consists of an evocative doctor-patient relationship permitting ventilation and reassurance, or more intensive uncovering therapy with hypnosis and intravenous barbiturates, if necessary. Suggestions of chronic illness must be avoided and group loyalties re-established as rapidly and completely as possible.

Kolansky and Cole²⁸ also summarize their observations at the Neuropsychiatric Center of the 4th Field Hospital in Korea during the winter of 1950. They report that the use of female nurses was abandoned because their presence connoted a "hospital atmosphere" that might be too readily utilized for escape or regression, and that the neuropsychiatric wards had to be isolated from the medical and surgical wards because of the "infectiousness" of psychogenic symptomatology. The average hospital stay at their facility was under three days and 65 to 70 per cent of their patients were returned to duty.

Caldwell, Ranson and Sacks¹⁰ discuss panic reactions, particularly with reference to home defense, and suggest that civilian casualties be treated much the same as those in combat personnel. The major causes of panic are discussed under the rubrics of tension and insecurity, imitative behavior, suggestibility, rumor, lack of preparation and training, and vivid sensory stimuli.

TREATMENT

Psychotherapy. There seems to be a growing recognition of the need to make psychotherapy available to patients financially or otherwise unable to receive individual therapy from psychiatrists, and recent British medical literature in particular urges the general practitioner to play a greater role

in the diagnosis and treatment of the neuroses. On the other hand, Rodger⁴¹ warns the practitioner to guard against transference complications and believes that therapy other than history-taking and ventilation should be referred to the well-trained specialist.

St. Clair⁴⁴ draws attention to the high rate of psychiatric illness among Negroes, and mentions several distinct features requiring special consideration in their treatment: e.g., the difficulty of establishing free rapport in the face of greater suspiciousness or submissiveness and the somewhat greater tendencies of the Negro to act out his problems. Nevertheless, the author emphasizes the fact that these differences are not racially but culturally determined.

Semantics. Kelley²⁷ reports excellent results in the treatment of selected war neuroses by Korzybskian procedures leading to symbol clarification, referent analyses, and operational reorientation. However, since Kelley excluded psychopathic personalities and conversion hysterics and also employed narcotherapy, sub-shock insulin, and group therapy methods, it is difficult to assess the individual effectiveness of his several technics.

Psychoanalysis. Stephen⁵⁰ and Miller³⁴ believe that obsessive-compulsive patients with a good sense of reality (present or potential) and a capacity for integration, growth, and mastery are the most apt candidates for analytic therapy regardless of the symptomatology leading the individual to seek help, but the authors question the invariable suitability of psychoanalysis for this form of neurosis. Alexander,² in tracing the therapeutic factors in psychoanalytic treatment, points out that the relationship between the patient and analyst is unique in that the latter is devoid of judgmental or emotional prejudices. This permits exploration of repressed and transference material and facilitates corrective emotional experiences, leading to the gradual recognition and rejection of neurotic patterns and progressive readaptations to reality.

Pharmacologic Aids. Tilkin⁵³ reports a follow-up study of the effect of pentothal interviews in anxiety states and stresses the utilization of this technic to shorten the time spent in therapy. Schein and Goolker⁴⁶ prefer pervitin (d-desoxy-ephedrine hydrochloride) to pentothal because the patient remains conscious, abreactions occur more swiftly, and transference relationships develop more rapidly. Monro and Conitzer³⁶ have also employed this drug in the depressive states but conclude that it cannot be used as a substitute for electro-shock therapy. Bustamante⁹ found that 40 units of insulin daily lessened the anxiety of his neurotic patients during concurrent psychotherapy.

Inhalation Therapy. Gilmour¹⁸ employs ether inhalations for procuring material inaccessible to barbiturate narcosynthesis but recognizes and discusses the dangers of this procedure. Baars,⁴ one of the few advocates of

Meduna's CO₂ technic, believes that it influences "pathologic reaction patterns" but does not in itself constitute a cure for neurosis.

Hospitalization. Smith and Smith⁴⁹ discuss the advantages of the hospitalization of neurotic patients manifesting anxiety as the predominant symptom, and infer that change of environment and better facilities for observation and treatment are the main advantages. Worden⁵⁷ discusses the psychotherapeutic utilization of authority in the hospital situation and concludes that the recognition of the need for realistic conformation is a prime requisite for psychiatric recovery. Miles et al.³² report that, of 62 cases of anxiety followed for from two to 12 years after hospital treatment, 23 per cent were markedly improved, 35 per cent definitely better, and 42 per cent essentially unchanged.

Group Therapy. Geller¹⁷ reports that only about half of the state hospitals in this country use group technics but that their utilization is on the increase. He is in essential agreement with Ackerman¹ as to the effectiveness of group therapy in the neuroses and the disabling forms of personality disorder, in which, according to the latter author, group procedures may be as effective as individual therapy.

General. Finally, Diethelm¹⁵ summarizes the viewpoint of many authors by proposing that modern psychotherapy need not aim to change the entire personality but should instead enable the patient to understand his anxieties, utilize his abilities, carry out his job, and go through periods of stress without becoming overly disturbed. With this in view, regardless of the method used, all therapy must be comprehensive and dynamic, and distinctions between "deep" and "superficial" methods are spurious except as to therapeutic and social goals.

REFERENCES

- ¹ Ackerman, N. W.: Psychoanalysis and group psychotherapy. *Group Psychotherapy*. 3:204-215, 1950.
- ² Alexander, F.: Analysis of the therapeutic factors in psychoanalytic treatment. *Psychoanalyt. Quart.* 19:482-500, 1950.
- ³ Alvarez, W. C.: *The Neuroses: Diagnosis and Management of Functional Disorders and Minor Psychoses*. Philadelphia, W. B. Saunders, 1951.
- ⁴ Baars, C. W.: The pharmaco-dynamic treatment of psychoneuroses by use of carbon dioxide inhalations. *Minnesota Med.* 34:51-53, 1951.
- ⁵ Bieber, I.: Pathological boredom and inertia. *Am. J. Psychotherapy*. 5:215-225, 1951.
- ⁶ Boisen, A. T.: The therapeutic significance of anxiety. *J. Pastoral Care* 5:1-11, 1951.
- ⁷ Bowman, K. M. and Rose, M.: A criticism of the terms "psychosis," "psycho-neurosis," and "neurosis." *Am. J. Psychiat.* 108:161-166, 1951.
- ⁸ Brown, E. A.: Nasal function and nasal neurosis. *Ann. Allergy*. 9:563-567, 1951.
- ⁹ Bustamante, J. A.: The use of insulin in small doses as a method to facilitate the

- action of psychotherapy in some psychoneurotic disorders. *Am. J. Psychotherapy.* 5:425-433, 1951.
- ¹⁰ Caldwell, J. M., Ranson, S. W., and Sacks, J. G.: Group panic and other mass disruptive reactions. *U. S. Armed Forces M. J.* 2:541-567, 1951.
 - ¹¹ Clausen, J.: Respiration Movement in Normal, Neurotic and Psychotic Subjects. *Acta psychiat. et neurol. Suppl.* 68. Copenhagen, Munksgaard, 1951.
 - ¹² Clow, H. E. and Allen, E. B.: Manifestations of psychoneuroses occurring in later life. *Geriatrics* 6:31-39, 1951.
 - ¹³ Cohen, M. E.: Studies of palmar hand sweat in healthy subjects and patients with neurocirculatory asthenia (anxiety neurosis, neurasthenia, effort syndrome) with a description of a simple quantitative method. *Am. J. M. Sc.* 220:496-507, 1950.
 - ¹⁴ Croft, P. G.: Some observations on neurosis in farm animals. *J. Ment. Sc.* 97: 584-588, 1951.
 - ¹⁵ Diethelm, O.: Evaluation of psychotherapy. *Digest Neurol. & Psychiat.* 19:105, 1951.
 - ¹⁶ Freeman, T.: Pregnancy as a precipitant of mental illness in men. *Brit. J. M. Psychol.* 24:49-54, 1951.
 - ¹⁷ Geller, J. J.: Current status of group psychotherapy practices in the state hospitals for mental disease. *Group Psychotherapy.* 3:231-240, 1950.
 - ¹⁸ Gilmour, D.: Ether: An estimation of its use in the treatment of the psychoneuroses. *J. Ment. Sc.* 97:148-158, 1951.
 - ¹⁹ Glass, A. J.: Combat exhaustion. *U. S. Armed Forces M. J.* 2:1471-1478, 1951.
 - ²⁰ Gordon, A.: Precipitating factors in neuroses and psychoses. *Arch. Neurol. & Psychiat.* 66:571-579, 1951.
 - ²¹ Gould, L.: Mirror of your mind. Hearst Publications daily column.
 - ²² Harris, I. D.: Mood, anger and somatic dysfunction. *J. Nerv. & Ment. Dis.* 113: 152-158, 1951.
 - ²³ Henry, J.: Family structure and the transmission of neurotic behavior. *Am. J. Orthopsychiat.* 21:800-818, 1951.
 - ²⁴ Hoagland, H.: Adrenal cortical function in psychiatric disturbances. *Digest Neurol. & Psychiat.* 19:67, 1951.
 - ²⁵ Kamman, G. R.: Traumatic neurosis, compensation neurosis or attitudinal pathosis? *Arch. Neurol. & Psychiat.* 65:593-603, 1951.
 - ²⁶ Karagulla, S.: Evaluation of electric convulsion therapy as compared with conservative methods of treatment in depressive states. *J. Ment. Sc.* 96:1060-1091, 1950.
 - ²⁷ Kelley, D. M.: The use of general semantics and Korzybskian principles as an extensional method of group psychotherapy in traumatic neuroses. *J. Nerv. & Ment. Dis.* 114:189-220, 1951.
 - ²⁸ Kolansky, H. and Cole, R. K.: Field hospital neuropsychiatric service. *U. S. Armed Forces M. J.* 2:1539-1545, 1951.
 - ²⁹ Malmo, R. B., Shagass, C., and Davis, F. H.: Symptom specificity and bodily reactions during psychiatric interview. *Psychosom. Med.* 12:362-376, 1950.
 - ³⁰ Margolin, S. G.: The psychosomatic approach to neurocirculatory asthenia; a supplement to the relation of neurocirculatory asthenia to anxiety neurosis. *J. Mt. Sinai Hosp.* 17:930-933, 1951.
 - ³¹ Masserman, J. H., Arief, A., Pechtel, C., and Klehr, H.: The effects of direct interrupted electroshock on experimental neuroses. *J. Nerv. & Ment. Dis.* 112:384-392, 1950.

- ³² Miles, H. H. W., Barrabee, E. L., and Finesinger, J. E.: Evaluation of psychotherapy with a follow-up of 62 cases of anxiety neurosis. *Psychosom. Med.* 13:83-105, 1951.
- ³³ — and Cobb, S.: Neurocirculatory asthenia, anxiety and neurosis. *New England J. Med.* 245:711-719, 1951.
- ³⁴ Miller, E.: Discussion on the treatment of obsessional neuroses. *Proc. Roy. Soc. Med.* 43:999-1001, 1950.
- ³⁵ Moloney, J. C.: A study in neurotic conformity: the Japanese. *Complex.* Spring, 1951. pp. 26-32.
- ³⁶ Monro, A. B. and Conitzer, H.: A comparison of desoxyephedrine (methedrine) and electroshock in the treatment of depression. *J. Ment. Sc.* 96:1037-1042, 1950.
- ³⁷ Neustatter, W. L.: The treatment of psychoneurotics. *Lancet.* 1:1331-1334, 1951.
- ³⁸ Oppenheimer, B. S. and Gertler, M. M.: The relation of neurocirculatory asthenia to anxiety neurosis. *J. Mt. Sinai Hosp.* 17:924-929, 1951.
- ³⁹ Ranson, S. W.: Psychiatric treatment in combat areas. *U. S. Armed Forces M. J.* 1:1379-1397, 1950.
- ⁴⁰ Ripley, H. S. and Wolf, S.: Studies in psychopathology; data concerning adaptation to the isolated situation of a combat zone in the Southwest Pacific. *J. Nerv. & Ment. Dis.* 114:234-250, 1951.
- ⁴¹ Rodger, F.: The management of the neuroses in general practice. *Glasgow M. J.* 32:48-49, 1951.
- ⁴² Rosen, V. H.: The role of denial in acute postoperative affective reactions following removal of body parts. *Psychosom. Med.* 12:356-361, 1950.
- ⁴³ Sacks, J. G.: Psychologic reactions to winter arctic conditions. *U. S. Armed Forces M. J.* 2:309-313, 1951.
- ⁴⁴ St. Clair, H. R.: Psychiatric interview experiences with negroes. *Am. J. Psychiat.* 108:113-119, 1951.
- ⁴⁵ Sargent, W.: Leucotomy in psychosomatic disorders. *Lancet.* 2:87-91, 1951.
- ⁴⁶ Schein, J. and Goolker, P.: A preliminary report on the use of d-desoxyephedrine hydrochloride in the study of psychopathology and psychotherapy. *Am. J. Psychiat.* 107:850-855, 1951.
- ⁴⁷ Seward, C.: Colonic pain and the colon neurosis. *Edinburgh M. J.* 58:17-28, 1951.
- ⁴⁸ Sherman, R. D., Zuska, A. J., and Madlem, L. S., Jr.: Combat neuroses. Papers read before the Philadelphia Psychiatric Society, Oct. 13, 1950. *Arch. Neurol. & Psychiat.* 65:647-649, 1951.
- ⁴⁹ Smith, H. B. and Smith, L. H.: Hospitalization in the treatment of the neuroses. *Am. Pract.* 2:241-246, 1951.
- ⁵⁰ Stephen, K.: Discussion on the treatment of obsessional neuroses. *Proc. Roy. Soc. Med.* 43:1002-1007, 1950.
- ⁵¹ Straker, M.: Surgical procedures and neurotic illness. *Canad. M. A. J.* 65:128-133, 1951.
- ⁵² Thompson, R.: The diagnosis and treatment of the neuroses in outpatient practice. *Practitioner.* 166:269-277, 1951.
- ⁵³ Tilkin, L.: Sodium pentothal in anxiety states; a follow-up study. *Dis. Nerv. System.* 12:304-306, 1951.
- ⁵⁴ Weigert, E.: Love and fear; a psychiatric interpretation. *J. Pastoral Care* 5:12-22, 1951.

- ⁵⁵ Wiggam, A. E.: Let's explore your mind. Daily column distributed by King Features Syndicate.
- ⁵⁶ Wittkower, E.: Acne vulgaris; a psychosomatic study. *Brit. J. Dermat.* 63:214-223, 1951.
- ⁵⁷ Worden, F. G.: Psychotherapeutic aspects of authority. *Psychiatry*. 14:8-17, 1951.
- ⁵⁸ Wortis, J.: Physiological treatment. *Am. J. Psychiat.* 107:519-523, 1951.
- ⁵⁹ Yap, P. M.: Mental diseases peculiar to certain cultures; a survey of comparative psychiatry. *J. Ment. Sc.* 97:313-327, 1951.
- ⁶⁰ Zahle, V.: On manic-depressive psychosis and neurosis. *Acta psychiat. et. neurol.* 26:95-110, 1951.

* Other chapters in this volume deal with this material more thoroughly. These 6 references are included here because of their closeness to the subject matter under discussion.

Psychosomatic Medicine

By EDWARD WEISS, M.D., LEON J. SAUL, M.D. AND
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THE necessity for the physical integration of psychiatry and general medicine is becoming increasingly recognized. Dr. A. E. Bennett¹ in numerous contributions has performed a real service in this regard. As he and his associates indicated in a recent survey, of 574,683 total beds, the 4,761 United States general hospitals provided only 24,000 beds for psychiatric patients—that is, only 4 per cent of all general hospital beds were used for psychiatric treatment. These beds accommodated only 1 per cent of all mental patients. The authors stated: "This is a strange situation, when emotional disturbances account for at least 25 per cent of all admissions to general hospitals, and mentally ill patients actually fill more than 50 per cent of all hospital beds."

The increasing appreciation of the role of emotional factors in many illnesses has made the general hospital the proper, necessary place in which to teach psychiatry and conduct research. Of 73 four-year medical schools in the United States, 52 used general hospitals for psychiatric teaching, training and research. Seventeen did not.

Voluntary health-insurance coverage of psychiatric disorders was seriously lacking. Only 10 per cent of Blue Cross and 5 per cent of Blue Shield plans studied provided the same benefits for psychiatric as for other medical disorders. The rest discriminated as to days, benefits, or dollar maximums. Half of the plans examined completely excluded psychiatric problems.

"The use of general hospitals integrates psychiatry into medicine, breaks down isolation, prejudice, and ignorance, and educates and benefits the community through early treatment of mental illnesses. Universal acceptance of psychiatry within general hospitals would finally come to grips with our number one national-health problem—chronic mental illness—by training much needed personnel, automatically raising standards of diagnosis and treatment, encouraging earlier and better care, overcoming the asylum concept of psychiatry, and, finally, relieving the overcrowding of state hospitals."

Approximately one-third of private practicing psychiatrists have no hospital affiliation for treatment purposes. The restriction to office practice,

together with the increasing public demand for psychiatric service, greatly handicaps both patient and physician. General hospitals are the only logical institutions which can remedy this situation by providing psychiatric facilities for certified psychiatrists. Therefore, general hospitals that accept their full community responsibility will include psychiatric services. They will provide a minimum of 60,000 beds for psychiatric patients in at least 1,600 general hospitals, with mental-health clinics in at least 3,500. "An awakening of the general medical and hospital-administrative professions to this challenge can accomplish the goal in a decade."

SYMPTOM STUDY

Three hundred patients suffering from relatively early psychosomatic illnesses were studied by Musser⁸ to determine the common and important bodily symptoms which correlated closely with the development of their emotional disorder, symptoms which might suggest the possibility of an underlying emotional disorder. All of the patients had thorough physical examinations and on no occasion was the influence of existing organic disease minimized. Persistent insomnia was present in 57 per cent of the patients, and was often the earliest manifestation of emotional difficulty. In 30 per cent of the patients who had recurrent headache, an emotional cause was rarely suspected initially. Many had received intensive treatment for chronic nasal sinusitis, allergic rhinitis, histamine cephalgia, and "atypical" migraine, and only after these approaches had failed was psychiatric investigation undertaken. Pain or aching in the muscles of the neck, back, chest, or extremities was a prominent presenting complaint in 43 per cent of the patients.

These symptoms were some of the early bodily manifestations of emotional disturbances and often were the only indications of the psychosomatic nature of a patient's illness. Musser concluded that when these complaints are present, a thorough investigation of the life situation and personality of the patient is indicated.

Employing the technics of psychiatric interviewing and hypnosis, Seitz¹³ attempted to develop an experimental method for investigating symbolism and organ choice in conversion reactions. Utilizing a patient who developed marked choreiform spasms and jerking of certain muscle groups, following the death of her son, Seitz made the attempt hypnotically to substitute other symptoms for the original conversion reaction. He found that certain psychodynamically and symbolically equivalent symptoms may replace the original conversion reaction, whereas other nonequivalent symptoms could not be substituted in this way. Nine pilot experiments were reported to illustrate the application of this method. It was possible to replace psychogenic chorea with blushing and with circumscribed areas of excoriated

pruritus. Pruritus alone, hyperhidrosis of the palms, and anesthesia of the scalp could not replace the chorea, although these symptoms would occur when given as posthypnotic suggestions. Further hypnotic experiments resulted in spontaneous symptom substitutions; nausea and vomiting occurred when warts were suggested hypnotically. Anesthesia of the scalp developed in place of suggested alopecia areata. When urticaria was suggested as a substitute for weeping, coryza and eczematous dermatitis appeared instead. Suggested vesiculation on the hand resulted in "accidental" injury in precisely the designated area.

In one of the important studies on adrenal function coming from Thorn and his associates, Renold et al.¹¹ noted adrenal cortical responses to standard exertion and added emotional stress, as measured by changes in circulating eosinophil levels, in healthy oarsmen training for an important race. Members of the Harvard varsity and combination crews were observed during a two-week training period and immediately before and after contests with Yale crews. The regular mode of life maintained during the period of observation offered a well controlled background for the study.

The authors conclude that in well trained persons emotional stress, alone or in combination with muscular activity, may lead to a highly effective adrenal stimulation and may represent a necessary link in the mechanism of adaptation. They suggest the practical application of the simple technic used by them as a screening device for the estimation of adrenal function under various conditions.

In an experimental study of hay fever, Holmes,⁴ Treuting and Wolff tried to find evidence of summative effects of life situations, emotional reactions, attitudes, and mixed ragweed pollen to the experimental production of the hay fever syndrome.

The nasal mucous membranes were observed directly through a nasal speculum and simultaneous information concerning life situation and emotional reactions were obtained. Subjects were observed in a room containing a known concentration of mixed ragweed pollen. They discovered that the intensity of hay fever coryza is enhanced if the nasal mucous membranes are assaulted by pollen in a setting of conflict and anxiety. They concluded that the character of the mucous membrane response in the hay fever syndrome appears to depend not only on the intensity of the nasal hyperfunction produced by the exposure of "sensitive" individuals to pollen, but on the magnitude and duration of the hyperemia, hypersecretion, and swelling in the nasal chambers provoked by other threats and assaults to bodily integrity. Of major importance among these etiologic factors is a life setting engendering conflict and anxiety.

Swartz and Semrad¹⁵ examined 1348 admissions to the Boston State Hospital. Three hundred and fourteen or 23 per cent were discharged as

nonpsychotic. Among 578 psychotic patients between the ages of 16 and 60 they found an incidence of psychosomatic disorders of 3.4 per cent as contrasted with 4.5 per cent in the non-psychotic group. They suggest, what has often been mentioned before, that it may be that psychosomatic disorders are in a sense a defense and a protection against a psychotic break—that, to a certain extent, either a psychosomatic or psychotic mechanism may prevail. They have the impression that psychosomatic and psychotic disorders are not only incompatible but that each is to a great extent mutually effective in excluding the other. Neither did they find any correlation between specific psychosomatic disorders and specific psychotic disorders.

Storment¹⁴ tried to determine by means of psychologic surveys whether the relationship between disease syndromes and personality profiles, as pointed out by Dunbar, could be corroborated. Using the Guilford and Guilford-Martin series of Three Personality Inventories, Storment studied the following patients: hypertensive, 25; rheumatic, 25; coronary occlusion, 8; arteriosclerotic, 19; and noncardiac, 13. He was unable to find objective verification of the hypotheses of Dunbar. Rather, the null hypothesis was supported.

CARDIOVASCULAR SYSTEM

Anxiety may be accompanied by electrocardiographic changes in the absence of demonstrable heart disease as demonstrated by Crede et al.³ In the report of a case of a man of 27, subjected to various experiments, certain physiologic disturbances due to anxiety were manifested by "abnormal" T waves, similar in contour to those seen in the pattern of left ventricular strain but they appeared and disappeared rapidly. The changes were observed in limb leads as well as in precordial leads. The mechanisms involved were not elucidated, but data were presented which indicate that the changes were not due to alkalosis, anoxemia, change in position of the heart and diaphragm, or autonomic imbalance. Tachycardia and increased blood pressure usually accompanied the T wave inversion, although on occasion they varied independently within moderate limits.

Psychologic and physiologic data obtained during a prolonged period of observation were described.

Recent studies of the cellular elements of the blood have revealed significant alterations in the numbers of polymorphonuclear leukocytes, lymphocytes, and eosinophiles in relation to life stress and following the administration of ACTH. Now, Schneider and Zangari¹² have investigated the physicochemical changes in the blood (clotting time, relative viscosity, erythrocyte sedimentation rate, hematocrit, and prothrombin times) as they relate to stress in the normal and hypertensive subjects.

In general, single blood specimens obtained from subjects with long-standing hypertension in whom the blood pressure was no longer subject to wide fluctuations showed clotting time and blood viscosity values to be within the accepted range of normal. However, in such subjects where it was possible through emotional stress to produce a further elevation of blood pressure the clotting time would shorten and the blood viscosity would increase. On the other hand, single blood specimens from subjects with early vasolabile hypertension in periods where they were in fact hypertensive, showed shortened clotting time and elevated blood viscosity. If it were possible through application of emotional stress to cause a further rise in blood pressure in these subjects, a further shortening of the clotting time and rise in blood viscosity could be obtained.

The authors speculate that these changes in the blood, which are most generally accompanied by a pressor response, represent a protective reaction pattern in man used during short transient periods of stress which is beneficial in that the likelihood of excessive blood loss is reduced (shortened clotting time) and added oxygen demands are satisfied (increased hematocrit and increased blood viscosity). However, it is also conceivable that if such a protective reaction pattern is chronically made use of, perhaps inappropriately, and there is suggestive evidence that this may be true in the hypertensive subject, then it may no longer be advantageous, but actually may become detrimental in that a shortened clotting time and increased blood viscosity may predispose to intravascular thrombosis, and the chronically elevated blood viscosity, by increasing peripheral resistance, may lead to increased need for cardiac work. The hypertensive patient is prone to develop coronary or cerebral thrombosis and, as noted above, shortened clotting time, increased blood viscosity, and an increase in hematocrit were nearly always associated with a pressor response.

The frequency with which emotional factors may play a significant role in influencing the course of hypertension has not been adequately clarified. Reiser, Brust and Ferris⁹ have rendered a service by summarizing their general observations concerning the relationship of emotionally stressful life situations to the course of hypertensive disease in 230 unselected patients. Special attention was paid to the natural course of the disease, the role of emotional factors, physiologic mechanisms involved, and the response of the patients to various pharmacologic agents and therapeutic procedures. The studies represented a multidisciplinary integrative approach, including the disciplines of psychiatry, internal medicine, surgery, pathology, and physiology.

The frequency with which the patients responded in a favorable manner to a sustained therapeutic relationship was quite striking and supported other evidence indicating the important role of emotional factors influ-

encing the course of hypertension. A majority of patients experienced marked symptomatic relief and functioned more effectively in their environment, and, in a period of observation which averaged 21 months, there was usually an absence of objective evidence of progression of the disease. In a small but significant percentage of patients an actual regression of structural changes and blood pressure levels was observed.

As part of a comprehensive study of hypertension, Reiser et al.¹⁰ investigated 12 patients who were in various stages of the transition from benign to malignant hypertension. In each of these patients, examination of the relationship between the life history and the medical course of the disease revealed that the precipitation of the malignant phase could be chronologically correlated with emotionally significant life situations or events. While psychosomatic correlations were specific within the individual patient, the data did not reveal any specificity of personality structure or conflict situations for the group as a whole and thus did not explain the selection of this organ system. "The findings are consistent with the view that the specific choice of the hypertensive vascular mechanism may be related to an additional factor, or factors, such as the presence of a predisposing renal lesion in patients with coexistent renal disease, but as yet unknown in the patients with essential hypertension."

Over the last several years, Cohen² and his associates have made many studies on "neurocirculatory asthenia" which they apparently hold to be synonymous with anxiety neurosis, neurasthenia, effort syndrome. In a recent publication they "summarize present day knowledge" on this subject. Their studies, which must have involved considerable effort and expense, and have extended over a period of years, are largely concerned with physiologic measurements and long term observations of the course of the "disorder." They have excluded psychodynamic observations as unscientific. In a criticism of these concepts, Miles and Cobb⁵ strongly disagree with this disregard of the importance of psychogenic factors in a well reasoned report which regards "NCA" and "Anxiety Neurosis" as opposite ends of a continuum, with the former diagnosis reserved for those patients who have evidence of a constitutional physiologic deficit. They conclude, and with this conclusion we agree, that "unless one makes some attempt not only to measure the constitutional or physiologic factors but also to understand the psychodynamics of the illness and of the therapeutic processes as well, it seems unlikely that even the most objective and scientific investigations can prove fruitful." They feel that the vagueness of the term, "neurocirculatory asthenia," when defined merely by a list of symptoms, results in confusion and increases the difficulty of interpreting research data. They urge that investigators whose interests and orientation are primarily physiologic should be more aware of the psychodynamic

differences among patients who resemble one another symptomatically. We question the term neurocirculatory asthenia which calls attention to a part of the organism rather than to the whole, and often leads physicians to feel that they understand the disorder because they have given it an imposing name. It would be much better to use the proper psychiatric designation and include qualifying phrases, for example, "anxiety hysteria with cardiac manifestations."

GASTROINTESTINAL TRACT

Szasz¹⁶ states that in accordance with the theory of the development of the libido, and also because of the anatomic structures involved, upper gastrointestinal disturbances have generally been interpreted in terms of oral regressions and lower digestive symptoms in terms of anal regressions, as symbolic expressions of unconscious psychologic content (giving, withholding). He believes that such formulations on dysfunctions of the lower gastrointestinal tract could be valid only for those cases of constipation and diarrhea in which the symptom is due to a disorder of the external anal sphincter. There are cases which do not express any primary psychologic meaning, but are manifestations of a vegetative (organ) neurosis, i.e., as the remote physiologic sequelae of oral tensions.

As an example, the author ascribes the symptoms of a patient to a persistent vagal excitation, leading in turn to inhibition of colonic and rectal activity, and finally to constipation. The interpersonal relationship in the analysis affected the patient's stomach as food affects the stomach of the infant, with a resulting feeling of satisfaction and increased vagal activity leading in turn to parasympathetic stimulation of the colon and rectum, and to defecation. In a patient with ulcerative colitis, attacks of diarrhea could be traced to an intense inhibition, on account of guilt, of powerful oral-sadistic (cannibalistic) tendencies; this psychologic "inhibition" is postulated to be paralleled by an inhibition of the vagi so that diarrhea results.

New concepts of gastric function have been derived from a detailed psychosomatic study by Margolin⁷ on a patient with a large gastric fistula. The patient was studied psychoanalytically. Physiologic observations were conducted independently. These included: (1) gastric motility; (2) color of mucosa; (3) volume of secretion; (4) quantitative determination of HCl concentration; (5) quantitative determination of pepsin concentration.

Margolin observed: (1) The functions of an involuntary organ, the stomach, are manifestations of unconscious mental states that can be objectively interpreted. (2) The relationship of these gastric functions to each other can be changed by altering the alignment of forces within the unconscious by psychoanalytic methods. (3) Given constellations in the

unconscious are repetitively and predictably associated with specific patterns of these gastric functions. (4) These facts serve as a method of verifying psychoanalytic data and of validating psychoanalytic theory.

Because of the prevalent occurrence of peptic ulcers in men, the psychosomatic approach to the syndrome has dealt chiefly with male patients. Now, Kezur,⁶ Kapp and Rosenbaum have studied twenty-five women with peptic ulcers from the psychosomatic point of view. All exhibited profound and overt personality disorders. The majority had been rejected by the mother and turned to the father for support. Ulcer symptoms were precipitated when the supporting figure, usually the husband, failed them. Oral aggressive feelings played an important role and were often equated with denial of femininity. This group of women with peptic ulcers had a much higher incidence of overt personality disturbances than the majority of a comparative group of male peptic ulcer patients previously studied, although frustration of dependent wishes was equally important in both groups. The shift in the sex ratio of peptic ulcer during the past 50 years suggests that cultural factors may play a role in the development of this disease.

REFERENCES

- ¹ Bennett, A. E., Hargrove, E. A., and Engle, B.: Psychiatric treatment in general hospitals. *J.A.M.A.* 147:1019-1023, 1951.
- ² Cohen, M. E. and White, P. D.: Life situations, emotions and neurocirculatory asthenia (anxiety neurosis, neurasthenia, effort syndrome). *Psychosom. Med.* 13:335-357, 1951.
- ³ Crede, R. H., Chivers, N. C., and Shapiro, A. P.: Electrocardiographic abnormalities associated with emotional disturbances. *Psychosom. Med.* 13:277-288, 1951.
- ⁴ Holmes, T. H., Treuting, T., and Wolff, H. G.: Life situations, emotions and nasal disease—evidence on summative effects exhibited in patients with "hay fever." *Psychosom. Med.* 13:71-82, 1951.
- ⁵ Miles, H. W. and Cobb, S.: Neurocirculatory asthenia. *New England J. Med.* 245:711-719, 1951.
- ⁶ Kezur, E., Kapp, F. T., and Rosenbaum, M.: Psychological factors in women with peptic ulcers. *Am. J. Psychiat.* 108:368-373, 1951.
- ⁷ Margolin, S. G.: The behavior of the stomach during psychoanalysis. *Psychoanalyt. Quart.* 20:349-373, 1951.
- ⁸ Musser, M.: Early diagnosis of emotionally conditioned illness, *J.A.M.A.* 147: 1030-1032, 1951.
- ⁹ Reiser, M. F., Brust, A. A., and Ferris, E. B.: Life situations, emotions, and the course of patients with arterial hypertension. *Psychosom. Med.* 13:133-139, 1951.
- ¹⁰ —, Rosenbaum, M., and Ferris, E. B.: Psychologic mechanisms in malignant hypertension. *Psychosom. Med.* 13:147-159, 1951.
- ¹¹ Renold, A. E., Quigley, T. B., Kennard, H. E., and Thorn, G. W.: Reaction of the adrenal cortex to physical and emotional stress in college oarsmen. *New England J. Med.* 244:754-757, 1951.
- ¹² Schneider, R. A. and Zangari, V. M.: Variations in clotting time, relative viscosity, and other physiochemical properties of the blood accompanying physical and

- emotional stress in the normotensive and hypertensive subject. *Psychosom. Med.* 13:289-303, 1951.
- ¹³ Seitz, P. F.: Symbolism and organ choice in conversion reactions. *Psychosom. Med.* 13:254-259, 1951.
- ¹⁴ Stormont, C. T.: Personality and heart disease. *Psychosom. Med.* 13:304-313, 1951.
- ¹⁵ Swartz, J. and Semrad, E. V.: Psychosomatic disorders in psychoses. *Psychosom. Med.* 13:314-321, 1951.
- ¹⁶ Szasz, T. S.: Oral mechanism in constipation and diarrhoea. *Internat. J. Psycho-Analysis.* 32:196-203, 1951.
- ¹⁷ Terhune, W. B.: *The Integration of Psychiatry and Medicine.* New York, Grune & Stratton, 1951.

Psychoanalysis

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THE self-scrutiny of the principles and practice of psychoanalysis continues to dominate developments in this field. Anna Freud's address at the commemorative program of Clark University, entitled "The Contribution of Psychoanalysis to Genetic Psychology"⁵ provides historical retrospect and pictures the present as a period of increasing understanding of ego functions. In attaining this goal she finds the "reformulation of analytic metapsychology in concepts of genetic psychology" by Hartmann, Kris, and Loewenstein particularly promising.

Discussing two important contemporary problems, she points to the intrinsic difficulties: (a) in subjecting analytic postulates to experimental verification and (b) in establishing a common language and sphere of collaboration with related sciences. Nevertheless, she finds encouragement from the fruitful effect that analysis has exerted on other fields of endeavor, particularly in child study.

Touching on the approach of psychiatric social workers and counselors to psychotherapy, she finds a tendency for them to borrow dynamic explanations from psychoanalysis, while looking askance at the essential genetic concepts. Consequently, new therapeutic technics evolve that differ characteristically from Freudian methodology; instead of seeking to recapture the repressed through the study of genetic data, dynamic solutions are sought in the present, regardless of the ultimate origin of the difficulties.

To illustrate basic differences she cites L. K. Frank that gentle treatment of the growing child will lead to learning without arousing feelings of resentment or aggression. Anna Freud finds such dispositions in the child dating from infancy. The management consists not so much in sparing the child conflicts that are largely inevitable, but rather in education toward adopting those solutions which best reconcile the ego and the id with each other and with the environment. Problem-setting for such purposes

should be neither too frustrating nor too sparing of the need to submit to social demands.

A similar conclusion is reached by Buxbaum² in a study of the latency period. She reports that reaction formations and obsessive-compulsive mechanisms play a necessary role in assisting the child to master his anxieties and insecurities. The well-oriented educator will wish to assist the youngster's spontaneous attempts to establish rules of conduct for himself; undue permissiveness, on the contrary, is experienced as a threat.

The genetic approach, especially with respect to its implications for therapy, received further attention during 1951 by Hartmann,¹⁰ Kris,¹² and Loewenstein.¹⁴ The latter, taking issue with the Chicago school, asserts that their attempts to shorten and simplify the analytic procedure by limiting themselves essentially to dynamic changes produced by interventions that minimize the use of interpretations, devalues "what is specifically psychoanalytic," i.e., dynamic changes produced by insight gained from interpretations. He discusses the principles of the latter in terms of ego psychology and introduces the term "reconstruction upwards" to describe the use of data for the pointing out of the relevant psychic reality—to transpose from a regressive level to a more superficial one. Material which obviously relates to deep levels is interpreted in connection with relatively recent pathogenic conflicts.

Kris¹² emphasizes the view that resistance is no longer regarded simply as an obstacle to analysis, but is part of the psychic surface itself. Various analysts operate at different degrees from the surface, a fact determined to a considerable extent by a "personal equation." Both intuition and planning enter into therapy.

Hartmann¹⁰ agrees that no complete set of rules for analysis exists and that the management of each patient by each analyst has individual experimental aspects. Ego psychology "means progress in the ways of understanding and dealing with the reality aspects of our patients' behavior." Tracing neurotic to real anxiety was one decisive step, opening the way to a better acquaintance with adaptation and its role in the neurotic as well as in the so-called normal individual. Hartmann outlines the concept of a "secondary autonomy" by which functional patterns attain a dynamic significance apart from their genetic origin. The effects of interpretation are so intricate and unpredictable, in the light of the complications of psychic structure, that their extension through the personality is determined by the principles of "multiple appeal."

This principle involves a limited use of the field concept. A process set in motion by a stimulus, i.e., interpretation, produces not only local reactions but affects the whole dynamic system, activating or preparing elements functionally and genetically connected with it. Its appeal often

reaches from one system to the other. Its unconscious side effects may overcome counter cathexes. Both structural and dynamic factors are involved.

The role of the analyst in assisting the patient to adapt is traced by Nunberg.¹⁷ Transference, he explains, is no mere recapitulation of the past but a seeking for solution of past problems in the present; consequently, it has value as a progressive force. Through the analytic work of demonstrating the irrational and past roots of behavior, reality-testing is enhanced.

The orientation of the patient to reality as an active auxiliary to genetic investigations is explored by Frumkes⁷ who, drawing upon the teachings of Ferenczi and Lorand, reports upon the use of advice and discussion of current problems as a means of diminishing frustrations and fixing character changes that have been initiated during analysis.

Devereaux³ discusses the effect of confrontation and interpretation in terms of effecting closures of Gestalts. Confrontations consist in directing the patient's attention to the bare factual content of his actions, statements, or unregistered coincidences. It serves as a starting point for new associations. Interpretation is a means of bringing to a head or resolving some hitherto insoluble problem. The crucial difference between the two is the overwhelmingly greater significance of psychic readiness for the effectiveness of interpretation.

K. Eissler⁴ and Wexler²³ discuss the dynamics of the therapeutic relationship and propose consequent methods of handling schizophrenic patients along analytically oriented lines. Eissler directs attention especially to the acute phases of the psychosis. He reports upon the value of manifestations of the therapist's real feelings, both libidinal and aggressive, as they are experienced through the deep unconscious mechanisms of the patient's mind, i.e., his primary processes. The best equipped physician for this purpose is one who is affectively determined to bring about a cure, has faith in his own powers, has a gift for dramatization and does not exercise undue inhibition over his own primary processes. In such terms, the miraculous cures of mental affliction reported in the Bible become understandable. Fromm-Reichmann,⁶ in a discussion of Eissler's paper, agrees as to the importance of the therapist's primary processes but feels that the focus in the treatment of the psychoses, as in the neuroses, centers on the anxieties of the patient in their therapeutic situation.

Wexler²³ also stressing the role of direct feeling in the treatment of schizophrenia, describes the "savage morality" of these individuals and believes that the therapist, by providing a nucleus of rudimentary super-ego identifications, assists the patient in controlling his inner chaos. Hatred, experienced in the counter-transference, is of great importance in this process and should be translated into and utilized in objective forms.

Problems of counter-transference are also considered by A. Reich²²

and Little.¹³ Reich reviews the boundaries between sublimation and acting out of the deeper personal motives involved in the therapist's wish to heal. Any disturbance of psychic equilibrium may shift the balance. Nevertheless, without a residuum of the original drives of the analyst, the necessary talent and interest in the task is lacking. Little adds that the analyst's fear of his own counter-transference creates a real danger and often leads to postponing or prematurely forcing termination. The sensitive patient will seek in turn to deny his own feelings, or will reveal to the analyst important information about the countertransference which should be heeded. The feelings of the therapist should be recognized, tolerated and applied effectively.

Spitz²⁴ reports on differences of development in white and colored infants after being brought up for one year under similar conditions in a nursery attached to a home for delinquent girls. The white babies showed definite superiority in intellectual and social capabilities. Not satisfied with any easy recourse to assumptions about racial factors, Spitz investigated this challenging situation and concluded that in the personalities of the mothers, who were in close contact with the children, lay the key to the problem. White girls who have lapsed from accepted social conventions are more likely to be repudiated by their families than are colored girls from a similar social level. Transgression in the colored girls had to be more severe to produce rejection and for them to be sent to the institution. As might be expected under such a selective process, the colored girls under study proved to have more disorganized personalities. These differences were reflected in the handling of the infants, creating corresponding reactions and character developments in the offspring. As Spitz points out, the role of the psychiatrist in remedying such a situation can prove only one of the factors at work in a social setting.

In a symposium on "The Cultural Factor in Psychoanalytic Treatment," Ackerman¹⁸ maintains that social tensions must affect the analyzability of the patient as well as the emotions of the analyst himself. He asks, "Is it not true that the adaptive strivings of the individual may become so bound to the irrationalities of certain dominant social patterns as to render therapeutic cleavage not only more difficult but sometimes impossible?" The struggle for adaptation reinforces certain defenses both in the patient and in the analyst, with consequent influence on technics, therapeutic goals and selection of cases.

Kardiner¹⁸ discusses the varying effects of culture on the expression of biologic functions. He points out that social maturity differs from sexual maturity and that one cannot conclude from the study of only one culture which facets are biologic and which cultural. *Feces* has different meanings in different cultures. The implications are not as clearly defined when both

analyst and patient are from the same culture as when they deviate, as with the Negro analyst and white analyst. With the deviant, transference and counter-transference difficulties must be dealt with. Freud had a cultural orientation, but since he derived it from sexuality, it remained biologically determined.

Mazer¹⁵ in a study of dreams induced during states of hypnosis, investigated their authenticity and relationship to spontaneous dreams during normal sleep. In contrast to the findings of M. Brenman,¹ he believes the hypnotic dream to be genuine and essentially the same in nature as other types but with differences in structure and function. The choice of dream symbols, which Mazer explores, shows the influence of the individual's personality and character.

Hendrick¹¹ reflects the increasing interest in very early object relationships. The pathology of psychosis and of many character problems is the result of a failure to develop integrated functioning during the time of the development of the ego. These "ego defect" neuroses are more closely related to the psychoses than the neuroses. Ego development itself arises out of very early "identification" with the mother. Identification is not possible until the child can differentiate himself from his environment. Development of the ego is learning how to deal effectively with the outer world, i.e., attain gratification and avoid pain.

Continuing his important series of studies, Rado²¹ evaluates depression from the adaptational point of view as a process of miscarried repair. A healthy person meets the emergency of a loss by calming his emotions, marshalling his remaining resources, and increasing his adaptive efficiency. In contrast, the depressed patient uses the incapacitating, regressive adaptive pattern of alimentary maternal dependence.

Three primary constituents are specific of the depressive spell: "The alternation of mood to one of sustained gloomy repentance, the regressive yearning for the alimentary security of the infant; and the struggle between the excessive emergency emotions, in which submissive fear defeats coercive rage." The first two are altogether peculiar to the depressive spell; the other is seen in obsessive and paranoid patterns.

"The depressive spell is a desperate cry for love, precipitated by an actual or imagined loss endangering security. Through expiatory self punishment the attempt is made to reconcile mother and to be reinstated in her loving care. In this process of emergency repair, the pain leads to activity designed to recapture lost pleasure. The inner picture is of the security felt while clinging to mother's breast. The infant's early fear of starvation is revived in morbid fears of impoverishment and in hypochondrical fears."

The use of repentance is complicated by the simultaneous presence of

resentment and by the attempts to force love through coercive rage. In this biting and devouring fantasies appear as well as reactive starvation. Unsuccessful rage leads to feelings of increased danger with increased self reproaches and self punishment. "The superlative bid for forgiveness may be suicide with the illusion of gaining mother's nourishing graces forever."

The patient takes pride in his coercive rage even after defeat has retroflected and forced this rage to subserve his repentance. His pride in his coercive rage, even after defeat, leads him to punish himself not only for his past defiance but also for his failure to coerce mother. The expiatory process is complicated by continued environmentally directed rage, often expressed in the form of ironic self reproaches.

In part, the extreme painfulness of depression is due to the simultaneous employment of conflicting submissive fear and coercive rage. The relative balance between fear and rage may determine whether retardation or agitation will ensue.

Prevailing problems of analytic therapy were the subject of panel discussions at the 1950 midwinter meetings of the American Psychoanalytic Association.²⁰ Lewin, Nunberg, Windholz and Waelder express in various ways the opinion, similar to Hartmann's, that basic insight into psychodynamics is the fundamental determinant of the course chosen by the analyst. Kubie questions whether ego psychology has brought any essential changes in technic and stresses the need for fundamental research into the nature of free association. He shows that assumptions underlying interpretations based on free association have frequently changed and comes to the conclusion that "the further progress of psychoanalytic technic and the whole development of psychoanalysis as a science waits on the development of some process either as an alternative to, or supplementary to, or as a corrective to, the haphazard processes of interpretation to which we are at present limited."

Sterba²⁵ does not feel that the mere process of interpretation is a sufficient vehicle for therapy. "There has to be some influence on the patient's ego on the part of the analyst in order to force the patient to do something with this interpretation. . . . Analysis implies suggestion (in the sense of) changing the outcome of the conflict." Pressure and re-education, he maintains, must supplement the genetic approach.

Johnson¹⁹ feels that there can be no sharp line drawn between analytic psychotherapy and analysis. There are only gradations of insight existing between a limited analytic psychotherapy, as practiced by the psychoanalyst, and a complete analysis. Discussing the problem of limited goals as fundamental in therapies short of thorough analysis, she finds it important to curtail the extent of regression and to decrease masochistic gratifications while increasing the pride and self-confidence of the patient. "It is far

easier," she declares, "to search for childhood memories than to perceive and make deductions from the wealth of detail in the patient's everyday experiences."

Stone,^{19, 26} in the panel discussion and also in a paper on brief psychotherapy, devotes attention to the utilization of psychoanalytic knowledge for treatment involving limited goals. Like several of the other commentators, he is impressed with the variety of technics employed by different analysts. He believes that such differences are highly instructive and asks, "Who knows that the 'wrong thing to do' may not have a special indication?" For brief psychotherapy, broad dynamic elements are more reliably estimated and more immediately useful than genetic reconstructions. Drawing upon his experiences in the clinic of the New York Psychoanalytic Institute, he formulates certain principles for guidance in brief psychotherapy. These include: (a) a concentration upon crucial problems within the framework of daily life; (b) a reliance on forces within the patient tending to spontaneous cure; (c) a combination of free association and active guidance in the interview; (d) utilization of relationships developed outside the transference. He expresses wonder that analysts, with their unrivalled insight into the human personality, do not more often make use of the potentialities of circumspect advice. From the standpoint of training candidates, he recommends as both realistic and helpful a greater latitude in permitting the use of psychoanalytic procedures in the early stages of their training.

In his attempts to define what he means by psychoanalysis, Stone²⁶ stresses the following: In general there is reliance on free association for communication. The procedure is guided largely by the patient's free associations from day to day. There is no immediate emphasis on curing symptoms. The analyst avoids giving advice and does not intervene directly in the patient's activities nor does he participate in the patient's daily life. The analyst attempts to be neutral and emotionally passive. By interpretation he helps the patient learn to understand the language of the unconscious. He uses occasional questions to help clarify issues. He provides certain psychologic information. At times, he reinforces the patient's ability to test reality through the use of his own impressions of situations.

But it is not merely by the use of his understanding of the patient's unconscious, important as such understanding may be, that the analyst functions. Stone believes that the technical aspects of psychoanalysis play an important part in making the treatment effective. Thus, he re-emphasizes regularity of time, frequency and duration of appointments. He feels that a minimum of three sessions a week are necessary, with a preference for a greater number. He also stresses the recumbent position for the patient with the analyst remaining in the background not directly

in the patient's view. If these technical details are materially altered, profound changes take place in the utilizability of the transference situation, especially in relation to the transference neurosis. Stone, as well as Gitelson,⁹ stresses the unique importance of the development and resolution of the transference neurosis in the analysis. This represents the re-enactment of the infantile neurosis in the analytic setting, and in their view is an essential element of the complete working out of the clinical neurosis in the treatment.

Stone notes again that the classical psychoneuroses remain the primary group of illness for which psychoanalysis is indicated.

Gitelson⁹ traces the influence of psychoanalysis on dynamic psychiatry. The latter he sees as a development of psychobiology profoundly modified by Freud's work. In attempting to demonstrate the differences between the working of the two methods of therapy, he places great emphasis on the development and use of the transference neurosis in the psychoanalytic situation.

He sees a rigid barrier between traditional and modified forms of psychoanalysis. While he finds place and even preferred indications for other types of psychotherapy, he visualizes manipulations of the classical procedure as attempts to repudiate and evolve a successor to psychoanalysis. The modern concepts of psychodynamics, he maintains, are inseparably bound up with established forms of psychoanalytic observation. He warns, "Somehow, in a successful analysis, the patient matures as a total personality. Somehow, a developmental process which has been halted or sidetracked, resumes its course. It is not insight; it is not the recall of infantile memories; it is not catharsis or abreaction; it is not the relationship to the analyst. Still, it is all of them in some synthesis which it has not been possible to formulate explicitly."

Gill⁸ discusses the implications of ego psychology on that type of psychotherapy which recognizes and rationally uses this recognition but does not analyze transference and resistance. Time-saving therapeutic methods leading to successful restoration of the previous integrative capacity of the ego should not be mistaken for methods which can effect radical changes in personality. Working through for such a change is a time-consuming process requiring the exposure of the resistances and of the neurotic impulses repeatedly and in their manifold connections. Since the behavior of the ego is an attempted solution of its problems in relation to all the psychic agencies and to the outside world, all of these aspects must be dealt with before significant change can occur. Finally, affective experience is necessary if the ego is to learn something deeply. This raises the question as to the relationship between the degree of development of the transference neurosis in the therapy and the extent of personality alterations possible. The

author concludes that knowledge of the functioning of the ego focuses recognition of certain unavoidable limitations of what can be accomplished in psychotherapy.

Miles, Barrabee and Finesinger¹⁶ in an important paper review the literature and compare previous evaluations of psychotherapy (including analysis). They present a follow-up study of 62 cases of anxiety neurosis with a discussion of the problems inherent in such a study.

The healthy trend among psychoanalysts to extend their knowledge, to improve their methods and to derive related methods of psychotherapy inevitably has raised many serious questions. The attempts to answer these have not been uniformly successful.

In the papers reviewed above, a number of authors have attempted to use the development of the transference neuroses as a differentiating criteria between true psychoanalysis and other derivative psychotherapies. Among psychoanalysts even of differing theoretic orientations this would not receive unqualified endorsement. The extent to which the transference manifestations organize is in part a matter of the type of illness and in part a matter of technic. Many analysts find that in the gradual working through of the transference manifestations, the necessary changes in the individual are effected and the illness overcome. In so doing, an organized transference neurosis may not develop, although all of the elements of the underlying disturbance may have passed in review.

Analysts are more in agreement on differentiating types of therapies in terms of whether the transference manifestations are used or whether they are subjected to thorough analysis. In psychotherapy, problems relating to transference may be recognized and utilized. In analysis they are analyzed until resolved in the mind. Many differences in psychoanalytic technic are possible, necessary and proper if the responses to them are recognized and carefully analyzed in the treatment.

More and more analysts are giving consideration to the nature of the real relationship between the patient and his therapist. There seems to be little doubt that the personality of the therapist, his counter-transference reactions and the nature of his technic influence the reaction of the patient over and beyond a simple repetition of infantile experience. Much that passes for transference resistance may be in part a product of the treatment rather than an inherent part of the illness.

Unsolved are many questions as to what must be worked through within the transference situation and at what point the individual is ready to tackle certain difficulties in real life. An extensive discussion of this problem will be found in chapter 27 of Volume VI of this series.

In resolving these highly technical problems, a particular attitude of mind on the part of psychoanalysts is required. The late John Rickman²³

states this in a quietly moving paper which should be read by all those interested in psychoanalysis.

"The concept of the transference situation is one of our great inheritances. It is a social situation demanding the utmost of the two participants, and it is to be expected that the use that is made of that research and therapeutic opportunity will never be quite the same in any two decades, or perhaps in any two years. It is also to be expected, and the event justified the surmise, that the inferences drawn from behavior in that situation will vary from individual to individual. A new idea, a re-viewing of an old idea, will change the pattern of behavior in that situation, if the idea is real, i.e., if it has effects.

"Transference (and counter-transference) deals with forces within the participants which have not established perfect equilibrium and are in conflict with one another. It is a situation which calls for constant vigilance. Vigilance is a part of the analyst's habit of mind. . . ."

Rickman goes on to discuss how scientific meetings can be made fruitful: "The differences in behavior in the transference situation which discussion discloses are one of the healthy signs of our work. . . . (Discussion) fails in usefulness if not guided by a friendly participation in the total situation being disclosed.

"Though differences in behavior in the transference situation are to be expected and their discussion welcomed, the institutionalizing of these differences must be undertaken with considerable caution by the group and with an equal hesitation by the individual. The corrective to institutionalize differences . . . lies in the conduct of the scientific discussions. . . .

"These require an understanding of the speaker's frame of reference with a full and lively sense of its potentialities as he himself feels them. Our meetings . . . can provide a climate favorable to the germination of ideas."

Rickman concludes with a quotation from Bacon: "It would be an unsound fancy and self-contradictory to expect that things which have never yet been done can be done except by means which have never yet been tried."

REFERENCES

- ¹ Brenman, M.: Dreams and hypnosis. *Psychoanalyt. Quart.* 18:455, 1949.
- ² Buxbaum, Edith: A contribution to the psychoanalytic knowledge of the latency period. Workshop, 1950. *Am. J. Orthopsychiat.* 21:182, 1951.
- ³ Devereaux, George: Some criteria for the timing of confrontations and interpretations. *Internat. J. Psycho-Analysis.* 32:19, 1951.
- ⁴ Eissler, K. R.: Remarks on the psycho-analysis of schizophrenia. *Internat. J. Psycho-Analysis.* 32:139, 1951.
- ⁵ Freud, Anna: The contribution of psychoanalysis to genetic psychology. *Am. J. Orthopsychiat.* 21:476, 1951.

- ⁶ Fromm-Reichmann, Frieda: Discussion of Dr. K. R. Eissler's remarks on the psycho-analysis of schizophrenia, with Dr. Milton Wexler. *Internat. J. Psycho-Analysis*. 32:238, 1951.
- ⁷ Frumkes, George: Types of activity in psychoanalytic technique. *Psychoanalyt. Rev.* 38:305, 1951.
- ⁸ Gill, Merton M.: Ego psychology and psychotherapy. *Psychoanalyt. Quart.* 20:62, 1951.
- ⁹ Gitelson, Maxwell: Psychoanalysis and dynamic psychiatry. *Arch. Neurol. & Psychiat.* 66:280, 1951.
- ¹⁰ Hartmann, Heinz: Technical implications of ego psychology. *Psychoanalyt. Quart.* 20:31, 1951.
- ¹¹ Hendrick, Ives: Early development of the ego: identification in infancy. *Psychoanalyt. Quart.* 20:44, 1951.
- ¹² Kris, Ernst: Ego psychology and interpretation in psychoanalytic therapy. *Psychoanalyt. Quart.* 20: 15, 1951.
- ¹³ Little, Margaret: Counter-transference and the patient's response to it. *Internat. J. Psycho-Analysis* 32:32, 1951.
- ¹⁴ Loewenstein, Rudolph M.: The problem of interpretation. *Psychoanalyt. Quart.* 20:1, 1951.
- ¹⁵ Mazer, Milton: An experimental study of the hypnotic dream. *Psychiatry*. 14:265, 1951.
- ¹⁶ Miles, Henry H. W., Barrabee, Edna L., and Finesinger, Jacob E.: Evaluation of psychotherapy. *Psychosom. Med.* 13:83, 1951.
- ¹⁷ Nunberg, Herman: Transference of reality. *Internat. J. Psycho-Analysis*. 32:1, 1951.
- ¹⁸ Panel: The cultural factor in psychoanalytic treatment. Chairman, Nathan W. Ackerman, M.D., Reporter, Clara Thompson, M.D. *Bull. Am. Psychoanalyt. A.* 7:319, 1951.
- ¹⁹ Panel: Psychoanalysis and psychotherapy. Chairman, Bernard Bandler, M.D.; Reporter, O. Spurgeon English, M.D. *Bull. Am. Psychoanalyt. A.* 7:252, 1951.
- ²⁰ Panel: Current problems of psychoanalytic technique: failures and results. Chairman, Robert Fliess, M.D.; Reporter, Norvelle C. LaMar, M.D. *Bull. Am. Psychoanalyt. A.* 7:229, 1951.
- ²¹ Rado, Sandor: Psychodynamics of depression from the etiologic point of view. *Psychosom. Med.* 13:51, 1951.
- ²² Reich, Annie: On counter-transference. *Internat. J. Psycho-Analysis*. 32:25, 1951.
- ²³ Rickman, John: Reflections on the function and organization of a psychoanalytical society. *Internat. J. Psycho-Analysis*. 32:218, 1951.
- ²⁴ Spitz, Rene A.: Environment versus races: environment as etiological factor in psychiatric disturbances in infancy. In *Psychoanalysis and Culture*. G. B. Wilbur and W. Muensterberger, pages 32-41. New York, International Universities Press, 1951.
- ²⁵ Sterba, Richard: Character and resistance. *Psychoanalyt. Quart.* 20:72, 1951.
- ²⁶ Stone, Leo: Psychoanalysis and brief psychotherapy. *Psychoanalyt. Quart.* 20:215, 1951.
- ²⁷ Wexler, Milton: Discussion of Dr. K. R. Eissler's remarks on the psychoanalysis of schizophrenia, with Dr. Frieda Fromm-Reichmann. *Internat. J. Psycho-Analysis*. 32:238, 1951.
- ²⁸ —: The structural problem in schizophrenia: therapeutic implications. *Internat. J. Psycho-Analysis* 32:157, 1951.

Also of Note

- Ackerman, Nathan W.: "Social role" and total personality. *Am. J. Orthopsychiat.* 21:1, 1951.
- Brierley, Marjorie: Trends in psycho-analysis. In *International Psycho-Analytical Library*, No. 39, edited by Ernst Jones. London, Hogarth Press and the Institute of Psycho-Analysis, 1951.
- Eisenstein, Victor W.: Differential psychotherapy of borderline states. *Psychiat. Quart.* 25:379, 1951.
- Freud, Anna: The Anna Freud lectures in America—1950. *Bull. Am. Psychoanalyt. A.* 7:117, 1951.
- Greenson, Ralph R.: On boredom. Abstract, *Bull. Am. Psychoanalyt. A.* 7:352 1951.
- Kaufman, M. Ralph: Psychoanalysis in medicine. *Bull. Am. Psychoanalyt. A.* 7:1, 1951.
- Kubie, Lawrence S.: The role of symbolic distortion in neurosis and psychosis. Abstract, *Bull. Am. Psychoanalyt. A.* 7:350, 1951.
- Lorand, Sandoz: *Clinical Studies in Psychoanalysis*. New York, International Universities Press, Inc., 1950.
- Margolin, Sydney G.: The behavior of the stomach during psychoanalysis. *Psychoanalyt. Quart.* 20:349, 1951.
- Masserman, Jules H.: Some current concepts of sexual behavior. *Psychiatry* 14:67, 1951.
- Miller, Emanuel: Discussion on the treatment of obsessional neuroses. *Proc. Roy. Soc. Med.* 43:999, 1950, as reviewed in *Digest Neurol. & Psychiat.* 19:171, 1951.
- Panel: Mania and hypomania. Chairman, Phyllis Greenacre, M.D.; Reporter, Rene A. Spitz, M.D. *Bull. Am. Psychoanalyt. A.* 7:265, 1951.
- Panel: On depressive states. Chairman, Phyllis Greenacre, M.D.; Reporter, Emanuel Windholz, M.D. *Bull. Am. Psychoanalyt. A.* 7:311, 1951.
- Panel: Problems of early ego development. Chairman, Margaret S. Mahler, M.D.; Reporter, Maurice Friend, M.D. *Bull. Am. Psychoanalyt. A.* 7:248, 1951.
- Potter, Howard W. and Klein, Henriette R.: Toward unification of training in psychiatry and psychoanalysis. *Am. J. Psychiat.* 108:193, 1951.
- Psychoanalytic Study of the Child*, Vol. VI. New York, International Universities Press, 1951.
- Saul, Leon J.: Inferiority feelings and hostility. *Am. J. Psychiat.* 108:120, 1951.
- Sperling, Melitta: The neurotic child and his mother: a psychoanalytic study. *Am. J. Orthopsychiat.* 21:351, 1951.
- Stephen, Karin: Discussion on the treatment of obsessional neuroses. *Proc. Roy. Soc. Med.* 43:1002, 1950, as reviewed in *Digest Neurol. & Psychiat.* 19:170, 1951.
- Stern, Max M.: Anxiety, trauma, and shock. *Psychoanalyt. Quart.* 20:179, 1951.

Projective Methods

By LEOPOLD BELLAK, M.D. AND DANIEL BROWER, PH.D.

FOR the purposes of this specific review of projective methods, and primarily for the benefit of psychiatrists, it may be useful to consider the exact place of these methods in the armamentarium of the doctor.^{13a}

The place of these methods is probably directly comparable to the function of clinical pathology and other laboratory methods (including x-ray) in general medicine. They are important aids in diagnosis and guides in therapy. The doctor should have enough familiarity with them to understand their differential indication and, at the same time, their limitations. It should be understood that, as in x-ray or other laboratory procedures, projective methods should not be relied upon or permitted to give one a slot-machine diagnosis. The psychologist's data should probably be best reported as "consistent with . . ." a given condition. It should be the clinician's task in either medical or psychiatric fields to integrate all the available test data with all the available clinical data and, only on the basis of this combination, arrive at a final diagnosis.

Projective methods examine a variety of functions, as was pointed out in last year's review of this publication. It may well be that the development will point principally in two directions: One set of functions may primarily contribute quantitative, formal diagnostic data; the other—primarily qualitative, content-variables. Pascal and Suttell's adaptation of the Bender-Gestalt Test²⁰ (which will be discussed further), is probably this year's outstanding contribution to the first function. They propose to measure Ego strength by their technic. The TAT and its modifications (MAPS Test), as illustrated in the Shneidman book²⁵ of this year, probably remains the outstanding representative of the content function. The Rorschach may contribute to either, depending upon the case and the working habits of the psychologist. However, essentially and originally, the Rorschach is a percept-analytic method more closely related to the "expressive" rather than to the "projective," and it is the former which permits the quantitative approach.

THE RORSCHACH TECHNIC

Hertz, one of the leading authorities in the use of the Rorschach test, published an extensive and critical review of 193 recent publications in the

Rorschach field.¹² She deals with validity, reliability, underlying theory, attempts at experimental verification, and special clinico-research problems.

Rosen²² tested the hypothesis that cards IV, VI, VII, and X of the Rorschach test are perceived by subjects as representing father-symbol, male-sexuality, mother-symbol, and family-symbol, respectively. He found considerable support for the first three of these but the family-symbol hypothesis received little support from the data. Even for the first three, the differences in the perception of symbolic meanings of the Rorschach cards are very wide. Accordingly, the Rorschach would appear to consist of stimuli "which have a partial, but not a total, symbolic communality for subjects."

With a view toward studying the phenomenon of "color shock" in the Rorschach, Meyer compared the protocols of a neurotic group with those of a control group.¹⁵ The neurotic group was given an achromatic Rorschach while the controls received the usual form of the test. "Color shock" is reported as not being due to the presence of color, *per se*, since certain responses were elicited from the achromatic test which might have been expected from the usual colored plates. More work is indicated along these lines, especially in investigating the hypothesis that color relates to affectivity in general.

Roe²¹ is continuing her investigations into the personality characteristics of scientists in various fields. This latest monograph comprises a very complete analysis of the personality traits generic to physical scientists.

The Rorschach test was used on a group of 66 child guidance cases by Salfield²³ in an attempt to determine the usefulness of the test in predicting treatment outcome. In only 5 per cent of the cases was there no correspondence between psychotherapeutic outcome and the Rorschach prognostication. In 63 per cent of the cases, a high degree of agreement between test prediction and clinical course is reported.

Eichler⁶ investigated the influence of a stress-produced anxiety state in the laboratory on the occurrence of 15 Rorschach factors which are generally viewed as anxiety signs. Through statistical analysis it was possible to differentiate those factors which stand up from those which do not stand up as significant differentiae of anxiety.

Palmer¹⁹ presents a carefully executed study on the Rorschach from a methodologic viewpoint. He submits the following essential hypotheses to study:

1. The validity of separate statements about personality, inferred from projective technics, depends upon the accuracy of the interpretation as a whole.

2. The test of validity of isolated statements is applicable to interpretations based on a dynamic, structural concept of personality.
3. The personality of the individual as inferred from the test protocol and from the criterion situation could be described by the same set of statements.

APPERCEPTIVE TESTS

The most brilliant summary of the problems of the TAT was made by Henry A. Murray in a brief presentation at the 106th meeting of the American Psychiatric Association.¹⁸ He emphasized the singular importance of clinical validation of the TAT, particularly by the psychoanalyst. He discussed his own method of avoiding merely descriptive stories. Dr. Murray requests the subject to look at the picture and then to put it aside. He then asks the subject to choose a name for the chief character before proceeding with the story and asks him to respond with as many outlines of plots to each picture as possible—thus hoping to gain a wider range of insight. Murray believes that something is lost by this procedure and the reviewer is also of the opinion that the spontaneity of responses may thus be interfered with. However, we believe it might be useful to have a subject tell a story—as heretofore—but to make it standard practice to ask for other possible plots—in the inquiry, after all, initial stories have been related.

Murray described two conflicting aims in current TAT development: one, to improve the stimulus value of the current set of pictures, and the other, to use a standard set of pictures (and to have standards for the present set). He proposes to solve this problem by means of a selection committee which would decide whether a new picture submitted for inclusion in the series is more effective than the one which it is to replace. Murray rejects length, vividness and dramatic intensity of the stories as criteria of value of the pictures. He believes that an adequate judgment can be made only on the basis of "extensive study of covert personalities of a large number of subjects who have taken the test." In Murray's own words, these would have to be investigations by psychoanalysts or by psychoanalytically trained investigators. Such work is not likely to come about spontaneously. Direction and planning will be necessary and nobody is in a better position and is a more appropriate person than Murray himself to initiate such a program.

In addition to an improved set of twenty or thirty cards for general use, Murray also suggests several special sets of four or five pictures each for testing specific areas currently unprovided for.

Schwartz, Riess and Cottingham²⁴ report another study of the Thompson Revision of the TAT, but this time within a wider and even more significant

frame of reference. Two mixed groups of colored and white students were tested by a white psychologist, and another group of white and colored students were tested by a colored psychologist. Five cards of the original TAT and five of the revised cards were used each time. It was found that the Negroes and whites in the north of the United States produce ideas in the TAT which are not significantly different in number regardless of which version of the TAT or which administrator was used. They again reject Thompson's overall assumption that Negroes would empathize more with the revised cards. Unfortunately, their paper did not give any significant results concerning the effect of the examiner-examinee relationship—a matter of the utmost importance and urgency of clarification.

Thompson and Bachrach²⁶ report on the experimental use of a set of chromatic TAT cards. They offer a theoretic discussion of expectancy of increase in productivity by the introduction of color and proceed to test their assumption on 110 students. The results suggest that in some instances color may increase productivity, though not unequivocally so.

Eriksen⁷ chooses as a point of departure some experiments on the relationship of need and perception to verify some well known clinical contentions concerning TAT data. He investigated the perceptual recognition threshold of his subjects for pictures of aggressive behavior (by means of tachistoscopic exposure) and also administered the TAT. He demonstrates that where "perceptual sensitization" occurs for aggressive stimuli, the TAT stories are manifestly aggressive in theme and content. Where "perceptual defense" against aggressive stimuli takes place, stimuli generally interpreted as objects of aggression are not so perceived and the stories are generally devoid of any aggressive content; blocking, lack of organization, and incoherence appear instead. Eriksen thus gives experimental verification for what often has been satirized as a "damned if you do—damned if you don't" judgment of clinicians: namely, if stories show abundance of aggression, this may be consistent with strong aggressive needs. On the other hand, if subjects fail to respond with aggression to stimuli in which one may expect it, the inference is drawn that the aggression is strong enough to be disturbing and is being dealt with by excessive repression.

The relationship of ambiguity of the stimulus to production is instructively investigated and discussed in a paper by Bijou and Kenny.⁴ They had 51 judges rank 21 TAT pictures for ambiguity. This invariably was defined in terms of the number of interpretations a picture permitted. One of their findings makes Murray's belief appear doubtful that the cards below ten permit less flight of fancy than those from eleven to twenty.

Eron and Ritter⁸ examined the possible differences between TAT's administered orally-individually and those obtained in a group in which

everyone wrote his own stories. Using two groups of 30 students each, they found that the oral stories were longer but that the quality and amount of thematic content was identical. The written stories had a somewhat happier tone and seemed to evoke much more "flippancy." In all, the authors feel that because of the similarity of the thematic content, it should be acceptable to use stories arrived at by the group method for the collection of thematic norms, in the way originally suggested by Rosenzweig.

Another junior offshoot of the TAT has appeared—the Michigan Picture Story Test. It consists of 21 photographs and is meant to be used with children of from 8 to 14 years of age. It thus overlaps in its lower range somewhat with the Children's Apperception Test, and in its upper range with the Symonds pictures for adolescents.

One paper by Hartwell, et al.¹¹ discusses the general background of the test, the careful selection of pictures and the establishment of some normative data. The approach to the story material seems to be predominantly—if not exclusively—formal with an attempt to evaluate clinical status by quantitative criteria as is discussed in the case of an eneuritic boy. The boy's responses in terms of popular objects (32), tense (of verbs: 74 per cent in the present tense), psychosexual variable (fixation at anal level and marked castration references), and "Direction of Force" (centrifugal) are considered as prognostically good in a way which does not seem very clear.

Another paper on the Michigan Picture Story Test, by Andrew, et al.³ is concerned with the establishment of the stimulus value of ten of the pictures and the investigation of developmental differences. Evaluation was made by means of two variables: "Level of Interpretation" and "Verb Tense." The authors rank stories from "no response" to "simple enumeration," etc., to "stories with antecedents and outcome," and assign each a score, the highest type of response meriting a value of twelve. The "Verb Tense" is concerned with the relative emphasis on the past, present, and future tense (the rationale behind the significance of which is not clear to this reviewer). The authors conclude that the "obvious content" of a picture has little relationship to either of the two variables and that this fact could be a basis for errors in clinical interpretation of projective tests without adequate normative data. With particular reference to the paper by Murray (discussed earlier) and his doubt as to the value of strictly formal characteristics as valid criteria of the stimulus value of a picture, considerable work will be necessary to decide such issues.

The Children's Apperception Test was used by Gurevitz and Klapper with schizophrenic and cerebral palsied children. They used a number of formal and dynamic variables to evaluate the responses and the pictures

and found that the test permitted a differentiation and illumination of the problems in each group.

A singularly ambitious project was undertaken by Shneidman, et al.²⁵ They sent the TAT and MAPS of a patient to 14 different psychologists known for their work with apperceptive methods (and other test data to other investigators), asking each to use his own method in interpreting the material blindly.

The result is a most informative book on the varieties of interpretation. The area of agreement is large, and the clinical data that are made available permit one to check the interpretations against them. It is possible that the record used was of more than average usefulness and that agreement on less dramatic stories might be less uniform. As Murray points out in his foreword to the book, the more rigid methods seemed—in this work—the less successful. The MAPS Test and the TAT seem to result in almost identical material, the MAPS, in some instances, giving the appearance of richer stories. A follow-up to the present study is expected in which each of the contributors to the present volume used the Q-Sorting Scheme for an expression of judgments. Also, prominent clinicians were sent the clinical material and were asked to use the Q-Sort. By this means it is hoped to arrive at some statistical measures of usefulness of projective method and clinical information.

Ammons, Butler and Herzig¹ have modified the TAT approach to vocational and personnel psychology, for use at either the guidance level or for business and industrial applications. This Vocational Apperception Test (VAT) portrays persons engaged in various occupations, e.g., teacher, doctor, lawyer, salesman, etc. For guidance purposes it is a question of to what extent the testee identifies himself with the figure indicated in a specific occupational role. Much more validation work is needed but this technic has definite possibilities.

MISCELLANEOUS TECHNIQS

The most comprehensive publication in the field this year is a book by Anderson and Anderson, "An Introduction to Projective Techniques."² It follows books by Bell and Abt and Bellak as the third major text exclusively devoted to projective methods and related procedures. There are 28 contributors to 24 chapters. Of the latter, three are introductory to the basic principles and problems of projective methods; the next chapters are dedicated to each one of the major methods; one chapter is on miscellaneous technics, two on the use of intelligence tests for personality appraisal, and four relate to various procedures of therapy.

Some critical remarks might be borrowed from one of the contributors, Van Lennep who, incidental to his excellent presentation of his Four-

Picture Test, discusses the concept of projection and protests the broadening of the concept of projection into meaninglessness. Graphology, psychodrama and intelligence tests can, of course, also lend themselves for projection, but need hardly be included among projective methods, *per se*, as they are in this book. Murray, who discusses the concept in his foreword, takes a similar exception to the confusion of projective, expressive and other variables.

Another major production of the year is Pascal and Suttell's²⁰ book on the Bender-Gestalt Test. They actually deviate from the original and narrow use of this test for gross pathology by considering the productions in terms of Ego strength. To copy the figures is a standardized task which they consider susceptible to quantitative treatment. This seems much more reasonable for this type of formal perceptual structure than for those of pictorial nature. The authors supply excellent illustrations for scoring, experimental data for their approach and an excellent manual for training and clinical use of their method.

A story-completion test for specific use with the physically handicapped was designed by Fielding.⁹ As the design of projective methods for specific areas of applicability is doubtlessly a useful and necessary matter, this seems a valuable procedure for a well circumscribed area of significance. It would be a mistake, however, to apply such specialized technics anywhere but to the specific indication. It should preferably be used in conjunction with a general personality test.

In a careful study involving the sentence-completion technic, Meltzoff¹⁴ demonstrated that the tone of the response is directly affected by the mental set of the subject, as determined by test instructions, as well as the tone, positive, negative, or neutral, of the stimuli, themselves.

Modell¹³ reports the use of human figure drawings as a means for investigating the personality changes that accompany psychotic regression and recovery. It was found that specific drawing changes were correlated with recovery from regressed states. These changes were described as body-image maturation and sexual maturation. These drawing changes were similar regardless of the type of psychosis or whether psychotherapy or physical therapies were used.

Giedt and Lehner,¹⁰ in using the Draw-A-Person technic, studied the relationship between the ages of two groups of subjects and the ages assigned by each group to male and female figures drawn. There were 188 male neuropsychiatric patients and 229 male college students. The authors report a constant, slight increase in ages assigned with increase in one's own age. However, at a certain age, the assigned ages change from being older than own-age to younger than own-age. Among the patients, this drop occurred for assigned age to female figures from 30 years on. Among

the students, it occurred for assigned ages to both male and female figures from 25 years on. This procedure, as part of the inquiry to the Draw-A-Person technic, serves to focus attention on the patient's *Weltanschauung*, i.e., does he structure his images predominantly in the past or in the future?

CLINICAL APPLICATIONS

Harrower and Kraus¹³ studied the personality characteristics of patients with multiple sclerosis. They found an overemphasis on dependency needs, a virtual absence of body-centered anxiety, a minimum of inner conflict or an attitude of resignation and an unrealistic tendency to see the world through rose-colored glasses. The authors have also approached the question of whether persons possessing these traits are more likely to develop multiple sclerosis or that the actual conditions of the disease process evoke these personality changes. They conclude that the psychologic changes, observed as the disease progresses, cannot be considered as predisposing the person to this disease. It seems rather that multiple sclerosis leaves its mark, to a greater or lesser degree, depending upon the patient's pre-morbid personality structure.

Brower and Oppenheim⁵ subjected a group of hospitalized psychotic depressions to an extensive psychologic battery before and after a course of electroshock therapy. This included, among others, the Rorschach, TAT, Figure-Drawing and Mirror-Drawing. Electroshock therapy seems to restore intellectual efficiency and orientation, rendering the patient more susceptible to external stimuli, both favorable (amenability to psychotherapy) and unfavorable (traumatic factors in the home or job situations.) The TAT seems to be eminently suited for the exposure of the predominant conflicts at work in the prepsychotic personality. It is in this area, and toward the goal of better reality functioning, that psychotherapy or psychiatric case work is sorely indicated in a follow-up capacity.

Another paper of clinical usefulness was offered by Meyer¹⁶ who discussed the use of projective tests in psychotherapy. He is particularly concerned with the effect of the prospect of being tested upon the patient (in terms of keeping or breaking appointments) and how testing affected the continuation of therapy. By examining extensive clinical records, he finds that testing does not have an adverse effect. He suggests seven contraindications to testing in order to avoid disturbing consequences: (1) Acute psychosis, incipient psychosis, or acute anxiety state. (2) Extreme difficulty in establishing relationships (where adjustment to an additional person would be an undue burden). (3) Likelihood that the patient will interpret referral for testing as disinterest on the part of the therapist. (4) Likelihood that the patient will interpret referral for testing as evidence of the incompetence of the therapist. (5) Patients who are afraid specifi-

cally of "test" situations in life and who have a tendency to run away from them. (6) Likelihood that the test situation might stimulate more material than seems desirable at the time. (7) If the therapeutic situation at the time of referral seems to make testing inadvisable—while testing might be advisable at a later, more suitable date.

These points seem to comprise the most careful consideration published thus far on the entire subject matter of the testing situation in relation to patient and therapist.

The overwhelming importance of improving the selection and placement of mental hospital ward employees has become increasingly apparent. Yerbury, Holzberg and Alessi²⁷ describe the use of the Revised Beta Intelligence Test and the Multiple-Choice Rorschach. Only slightly positive results were obtained in differentiating the good from the poor groups. A more extensive battery of tests might be more fruitful.

In conclusion, this year has occasioned a growing awareness of the need for more validation-experimental studies, on the one hand, and extensive studies of clinical applications, on the other, rather than the mere proliferation of new technics.

REFERENCES

- ¹ Ammons, R. B., Butler, M. N., and Herzig, S. A.: *The Vocational Apperception Test*. Louisville, Ky., Southern Universities Press, 1951. Set of 18 plates and manual.
- ² Anderson, H. H. and Anderson, G. L.: *An Introduction to Projective Techniques*. New York, Prentice-Hall, 1951.
- ³ Andrew, G., Walton, R. E., Hartwell, S. W., and Hutt, M. L.: The Michigan Picture Test: The stimulus values of the cards. *J. Consult. Psychol.* 15:51, 1951.
- ⁴ Bijou, S. W. and Kenny, D. T.: The ambiguity values of TAT cards. *J. Consult. Psychol.* 15:203, 1951.
- ⁵ Brower, D. and Oppenheim, S.: Effects of electro-shock therapy as revealed by psychological tests. *J. Gen. Psychol.* 45:171, 1951.
- ⁶ Eichler, R. M.: Experimental stress and alleged Rorschach indices of anxiety. *J. Abnorm. & Social Psychol.* 46:344, 1951.
- ⁷ Eriksen, C. W.: Some implications for TAT interpretation arising from need and perception experiments. *J. Personal.* 19:282, 1951.
- ⁸ Eron, L. D. and Ritter, A. M.: A comparison of two methods of administration of the TAT. *J. Consult. Psychol.* 15:55, 1951.
- ⁹ Fielding, B. B.: "A Story Completion" for use with the physically handicapped. *J. Proj. Techniques.* 15:299, 1951.
- ¹⁰ Giedt, F. H. and Lehner, G. F. J.: Assignment of ages on the Draw-A-Person Test by male neuropsychiatric patients. *J. Personal.* 19: 440, 1951.
- ¹¹ Hartwell, S. W., Hutt, M. L., Andrew, G., and Walton, R.: The Michigan Picture Test. *Am. J. Orthopsychiat.* 21:124, 1951.
- ¹² Hertz, M. R.: Current problems in Rorschach theory and technique. *J. Proj. Techniques.* 15:307, 1951.
- ¹³ Harrower, M. R. and Kraus, J.: Psychological studies on patients with multiple sclerosis. *Arch. Neurol. & Psychiat.* 66:44, 1951.

- ^{13a} Hoch, P. H. and Zubin, J. (eds.): *Relation of Psychological Tests to Psychiatry*. New York, Grune & Stratton, 1951.
- ¹⁴ Meltzoff, J.: Effect of mental set and item structure upon response to a projective test. *J. Abnorm. & Social Psychol.* 46:177, 1951.
- ¹⁵ Meyer, B. T.: An investigation of color shock in the Rorschach Test. *J. Clin. Psychol.* 7:367, 1951.
- ¹⁶ Meyer, M. M.: The direct use of projective techniques in psychotherapy. *J. Proj. Techniques.* 15:263, 1951.
- ¹⁷ Modell, A. H.: Changes in human figure drawings by patients who recover from regressed states. *Am. J. Orthopsychiat.* 21:584, 1951.
- ¹⁸ Murray, H. A.: Uses of the TAT. *Am. J. Psychiat.* 107:577, 1951.
- ¹⁹ Palmer, J. O.: A dual approach to Rorschach validation: A methodological study. *Psychol. Monog.*, No. 325, 65:1, 1951.
- ²⁰ Pascal, G. R. and Suttell, B. J.: *The Bender Gestalt Test*. New York, Grune & Stratton, 1951.
- ²¹ Roe, A.: A psychological study of physical scientists. *Genet. Psychol. Monogr.* 43:121, 1951.
- ²² Rosen, E.: Symbolic meanings in the Rorschach cards: A statistical study. *J. Clin. Psychol.* 7:239, 1951.
- ²³ Salfeld, D. J.: The usefulness of the Rorschach Test for diagnosis, prognosis and epicrisis, mainly in child guidance treatment. *J. Ment. Sc.* 97:84, 1951.
- ²⁴ Schwartz, E. K., Reiss, B. F. and Cottingham, A.: Further critical evaluation of the Negro version of the TAT. *J. Proj. Techniques.* 15:394, 1951.
- ²⁵ Shneidman, E. S., Joel, W., and Little, K. B.: *Thematic Test Analysis*. New York, Grune & Stratton, 1951.
- ²⁶ Thompson, C. E. and Bachrach, A. J.: The use of color in the TAT. *J. Proj. Techniques.* 15:173, 1951.
- ²⁷ Yerbury, E. C., Holzberg, J. D., and Alessi, S. L.: Psychological tests in the selection and placement of psychiatric aides. *Am. J. Psychiat.* 108:91, 1951.

Group Psychotherapy

By S. R. SLAVSON, EMANUEL HALLOWITZ AND LESLIE ROSENTHAL

INTRODUCTION

ONE of the major developments in the field of group psychotherapy during 1951 was the inauguration of the International Journal of Group Psychotherapy¹⁻⁴ by the American Group Psychotherapy Association. The Journal aims to reflect the various points of view and practices in the field of group psychotherapy. The Association intends to prevent the Journal from becoming a representative of a specific school of thought or individual, but rather to develop it into a mirror of the field of group psychotherapy in its many ramifications and applications. Two other developments reflecting the acceptance of this form of treatment in the field of psychiatry was the inclusion of sessions in group psychotherapy at the first International Conference on Psychiatry in Paris and the International Conference of World Federation for Mental Health Organization in Mexico.

THEORY

In a discussion on the psychoanalytic basis of group psychotherapy, Powdermaker⁵² traces general development of personality in relation to the family. She then attempts to indicate some of the dynamics emanating from psychoanalytic theory in relation to the interaction of the members to each other in a therapy group. She states that the infantile relationships and projections are increased in groups and that members play various and different roles in relation to each other. The fact that the group has a social organization has therapeutic importance because it gives a social reality which provides a "constant opportunity for reevaluation of the group's and individual's ideas and values". A group cannot tolerate the hidden or overt attack on the members' defenses.

Frank and Ascher²⁰ state that psychotherapy should have as its goal the modification of noxious attitudes; if successful, it will enable the patient to secure satisfactions with least disturbance to others and with a minimum of anxiety within himself. Emotional experiences that bring about changes in attitudes seem to be facilitated by certain therapeutic processes: "(1) support, (2) stimulation, (3) reality testing." Two accounts of cor-

rective emotional experiences are presented and the dynamics of support, stimulation and reality testing are thus illustrated.

Foulkes¹⁹ states that for group work to be group psychotherapy, three conditions must be fulfilled: (a) verbal communication and formulation are the principal occupation of the group; (b) such treatment must do full justice to the individual members and their interaction; (c) the therapist who has a group before him will want to avail himself particularly of the forces which present themselves in that situation. The author believes that the group analytic method observes these principles in a particularly pure form and that the group itself is a common matrix inside of which all other relationships develop. Therefore, everything that occurs in a group involves the group as a whole as well as each individual member. In another paper, Foulkes¹⁸ analyzes the role of the group therapist in his dynamic relationship to group processes.

Wender⁶⁷ reviews some of the early group influences in society and explains the psychodynamics involved. In discussing the development of group psychotherapy he contrasts it with the development of individual psychotherapy and finds that it has gone through many of the same stages. From the use of suggestion, contagion, authority, etc., group and individual treatment have progressed to free association, insight through interpretation, reality testing, etc. The former technics are now seldom used.

In discussing the current trends, Slavson⁶⁸ indicates that the present state of development of group psychotherapy makes it possible to divide the discussion under four headings: specificity, organicity, integration and research and evaluation.

Under the first, the authors shows that group psychotherapy as a treatment procedure can be designed and evaluated in terms of its specific application, i.e., children, adolescents or adults, as well as the particular setting, i.e., a child guidance clinic, out-patient clinic for adults, general hospital setting or mental hospital. He also points out that group psychotherapy is now adapted to specific clinical entities such as psychosis, psychoneurosis, delinquency, epilepsy, senility, aphasia, allergies, tuberculosis and hypertension cardiac illnesses.

Under organicity, Slavson indicates that there is "gradually evolving an organized body of knowledge, theory, nomenclature and practices characteristic to itself." While there is currently a considerable divergence of points of view and practices, the author believes that we can anticipate greater uniformity and agreement concerning the basic understandings of theory and practice. He describes a number of the major schools now in existence in which he sees a basic uniformity and convergence of opinion.

Under integration, the author points out that group therapy is now accepted as a part of individual psychotherapy as well as in other settings

such as hospitals or clinics, and that it is an integral part of the current literature dealing with clinical practices.

The confusion in present research and evaluation is pointed out; it is shown that the situation under which group therapy is practiced at the present time does not favor reliable research. Rather, only evaluation can be done at the present time. The author expresses the hope that some day facilities and a setting suitable to research will be created.

Schindler⁵⁸ discusses the therapy group as a manifestation of family patterns; the therapist plays the role of the parent, while the other members of the group are brothers and sisters, and he also shows how they act out these roles in the group. Schindler draws some of the conclusions from general sociology and supplies illustrations from folklore and folk languages, such as "Little Mother Russia" and "Little Father Czar." He indicates that "society is essentially a mother symbol and, therefore, feminine, while the State is essentially a father symbol and, therefore, masculine."

Bry⁹ lists forms of resistance that appear in therapy groups among which are protective talking, selective silence and laughter. She also describes character resistance such as acting out in a group and gives a detailed outline as to the types of groups and occurrences of resistance. She concludes that there is a great deal of similarity in the manifestations of resistance in individual and group psychotherapy. The character resistances are modified through the group situation because acting out is more frequent; the form and intensity of resistances are not affected by sexual, but rather by diagnostic, heterogeneity, as well as by type of leadership. The group itself handles many problems of resistance without the need of intervention by the therapist.

In discussing the relations of group psychotherapy and social anthropology, Mead⁴⁵ finds that like all group living, group therapy has to be related to the culture in which it is practiced and draws examples from the situation in Russia as compared to that in the United States, where the attitude toward the group and the possibilities for self-revelation are at variance. Therefore, the group constitution and practices would have to be changed as well.

A group is not merely a collection of individuals with a common purpose. In a true group, according to Powell,⁵³ there is not only a common purpose but there is a sharing in the achievement of the members' individual aims. The outstanding characteristic, however, is interaction. In a true group we find individuals coming together to pool their strengths and resources in order to accomplish something which none of them could achieve alone. Another characteristic is that the character of the group is determined by the character of its members, and is directly modified by the presence or absence of any one of them.

Catharsis, according to Slavson,⁶² enables us to bring to consciousness the repressed, guilt-provoking and anxiety-inducing feelings, thoughts and strivings. Through catharsis the patient is able to regress to that stage of emotional development where arrest or fixation occurred; when these fixation points are broken down the patient can make a satisfactory inner and social adjustment.

Two forms of resistance that patients will employ in group psychotherapy are "deflection" and "escape." They have special value in that they reduce anxiety and fear. However, should they be employed too often the therapeutic process may be vitiated or blocked. Some of the dynamics that accelerate catharsis in group psychotherapy are: (1) catalysis, (2) mutual support, and (3) universalization.

The therapist's task is to encourage catharsis and regression. The therapist must, therefore, be keenly attuned to the anxieties and fears of his patients and be constantly sensitive to the latent content and direction of the group interviews. He needs to help the patients overcome their resistance through the appropriate use of transference and by giving support. He may, according to the total situation, analyze the resistance of the group, incite or facilitate expression of hostility to himself, or reassure the members of the group of his acceptance of them. The strategem of deflection and escape can also be employed by the therapist when he becomes aware of rising anxiety in the group members which may be contraindicated at a given moment.

In another paper, Slavson⁶⁴ points out that the basic dynamics of all psychotherapy are present also in this form of treatment. He divides this practice into three types: play group psychotherapy, activity-interview group psychotherapy and interview group psychotherapy. Each of these is designed to meet the needs of patients of different clinical categories and ages. The first two are suitable for children between the ages of four and ten, while the last is used in the treatment of adolescents and adults. He further describes libidinal, sibling and identification transferences as well as the dilution of transference that occurs in group psychotherapy.

Catharsis, according to the author, is aided by universalization and deflected aggression as well as through target multiplicity and catalysis. In the transference relation, the presence of cathexis displacement plays an important role in group therapy as well as in individual psychotherapy and he outlines the differences between derivative and direct insight that occur in groups. The various types of catharsis, such as binding, libido-evoking and libido-revealing, the difference between the activity and verbal catharsis and their significances are discussed. According to the author, activity catharsis in the adult could be a form of resistance. The resistances men-

tioned are lateness, absenteeism, distraction, displacement, deflection, abruptness and silence.

Concerning the selection of patients, Wender⁶⁸ comes to the conclusion that there is a difference between the intra-mural and extra-mural patients. The needs of these patients are different and the settings of the treatment are at variance. However, with some explanations, "all patients should be allowed to come to group psychotherapy," since the author sees special values that can be derived from relationships in groups even for those patients for whom individual psychotherapy is indicated.

McDonald⁴⁴ states that "self-revelation as a means of masking a more fundamental problem at a given moment presents a greater difficulty in groups than in individual treatment." After discussing the various means of self-revelation, of advice-giving, positive and negative transferences and counter transferences, anonymous contributions and silences, the author states that the mask is frequently a springboard or a stepping stone to a significant problem; one must be aware of it as an indirect expression of more important problems with which the patients are preoccupied.

Prados⁵⁴ found that the use of films in group psychotherapy was very effective in overcoming resistance; it effected a deep impact on the unconscious system by efficiently shaking the barrier of repression. Regression to still more infantile levels was made possible and the therapist became a "loving mother." Following the film there must be sufficient time for patients to abreact all the affects that were stirred up by the film. If the discussion lasts long enough the patients begin to recite their own associations and bring to consciousness repressed infantile memories.

In another paper, Prados⁵⁵ emphasizes that group therapy is especially valuable in helping the individual gain insight into his defense mechanisms. As a result of the dynamic processes existing in the group, narcissistic barriers are broken down, thus making it easier to deal with many resistances that would prove more difficult to recognize and handle in individual sessions.

By the use of a questionnaire technic and the study of verbatim records of group discussions, Prados has been able to recognize objectively the influence the motion picture technic has had on therapeutic progress of patients. Some of these influences were: (1) Mobilization of memories which had been forgotten, (2) Modifications of patients' attitudes in some situations of everyday life immediately afterward, (3) Identification with different characters in the picture enabling patients to understand their own inner motivations and conflicts.

Mann⁴² offers some general observations on the dynamic processes occurring in therapy groups. He states that there are no qualitative differ-

ences between therapy and "normal" groups but rather the differences are quantitative. They manifest themselves chiefly in the more ambivalent feelings of the therapy group members toward the leader and toward each other.

In the therapy group there are many conflicting emotional currents: resistance toward change, ambivalence to the therapist, rivalries, etc., which make the work of the therapist more difficult. The therapist, to be effective, must understand the psychoanalytic concepts of anxiety, hostility, transference and countertransference and be able to recognize their manifestations as they occur in the group.

Frank²¹ outlines some of the difficulties in conducting research in group psychotherapy. The main difficulty he visualizes in the categorizing approach lies in the fact that it depends so much on the knowledge of the process that is being categorized. Another difficulty lies in the attempts to classify patients' behavior and the understanding of the meaning and attitudes underlying this behavior. The author also points out the difficulty of categorizing the therapist's activities and his intervention in the therapeutic process of the group. Because the group forms a complex pattern or a Gestalt, many factors are in operation; which of these each patient uses becomes a complicated procedure, presenting almost insurmountable difficulties for research. It is necessary to consider the "total situation" if any reliable principles and understandings can be derived from a research effort in this field.

Peck⁵⁰ re-examines some of our theoretic formulations concerning the therapeutic dynamics of group psychotherapy. He cautions against applying only the theories of individual treatment to the group processes as this will not allow for the broader implications inherent in this treatment method.

GROUP PSYCHOTHERAPY WITH PSYCHOTIC ADULTS

Lawton³³ describes out-patient group psychotherapy with convalescent schizophrenics at Brooklyn State Hospital. The program was evolved to meet the needs of those patients who, after intensive in-patient group psychotherapy, had achieved symptom remission but were left with a troubled awareness of conflicts. Groups were mixed, continuous and maintained at a size of fifteen. Inter-member communication was facilitated through the therapist's passivity; at times, members chose their own leader for specific sessions.

Fidler¹⁶ discusses the concept of therapeutic levels in group therapy with psychotics. The therapeutic level is defined as related to increasing influence upon the attitudes and tension of the patient. Free group discussion and

interchange, as in activity and analytic group, is seen as affording greater opportunity for understanding of unconscious mechanisms than the lecture or directive type of group. As in other treatment media, deeper personality levels can be reached only after handling of initial anxieties and resistances.

Gabriel²³ reports on the treatment of a borderline psychotic woman in analytic group psychotherapy; deeply significant material and unconscious fantasies relating to crucial familial figures were uncovered. The existence of prevalent attitudes of pessimism toward the psychotic patient is deplored by Breckir.⁸ Since the psychotic has lost his group and his society, the social values inherent in the group situation afford a new therapeutic channel toward recovery in which the therapist is the catalytic agent in helping to bridge the gap between the patient and his environment. The author emphasizes the proven fact that the psychotic responds positively to the social setting of group therapy where isolating defenses are lowered.

Glenn²⁶ outlines the use of group discussions to improve relations between patient and personnel in a mental hospital ward. "Round Table Psychotherapy" was developed by McCann and Almada⁴³ at a state hospital in St. Joseph, Missouri. This group therapy technic is designed to treat large numbers of patients. In the eleven months that this technic was employed, 16 of the original 25 had been released from the hospital. There is no conclusive proof that the round table technic of group therapy was responsible for this, although it seems likely that it played a significant role.

Luchins³⁹ reports on one of the procedures introduced into the sessions of five therapy groups for psychotic veterans. Playbacks of recordings of the whole or parts of a group or individual session were used with a selected member giving his impressions of other members, group members expressing their opinion of what other members thought of them, etc. These expressions were used as a basis for discussion. Discrepancies between what a patient thought another patient thought of him and the actual thoughts of that patient were subjected to group examination and study. The role each person played in the group and its effect on the others were also subject to discussion. This procedure seemed to help some patients to be more aware of the structure of social situations and of the roles he and others play in these situations. Further it seems to develop an understanding of the bases of their impressions of others and others' impressions of them.

An experimental group guidance program educative and informative rather than therapeutic, was begun in the convalescent care department of Manhattan (New York) State Hospital in November 1948. Kusch and Lucas²⁷ state that the aim of the program was to give patients and relatives a clearer understanding of the nature of mental illness, its management and the problems that might arise both during and after hospitalization.

In a follow-up interview study it was found that patients felt relieved through sharing common problems in the group. In a controlled study it was found that those patients who had participated in the group guidance program made more requests for services and appointments than did patients in the control group during convalescent care. In general, it was felt that the group guidance program should be expanded to include all suitable new admissions to psychiatric hospitals.

Standish and Semrad⁶⁵ report on five years of experience with group psychotherapy at the Boston State Hospital. Initially, the greatest obstacle to developing a program of group psychotherapy was to be found in the therapists themselves. Groups of 12 to 15 patients, meeting twice weekly for an hour duration, produced optimal results. Group therapy with psychotics passes through definite stages: (1) testing out of the situation. This is characterized by hostility to the hospital and its representatives. As this is worked through, it leads to (2) the expression of anxiety laden psychotic material. Gradually the material becomes more personal and leads to (3) introspection, mutual criticism and the working through of some of their emotional problems. The fourth closing phase is not entirely clear but in those patients who show most improvement, the therapist notes that they now begin to talk of future plans. Sixty-five per cent of the acute patients treated in group psychotherapy were on home visit as compared to 34 per cent of the chronic patients.

Menzer, Irvine and Semrad⁴⁷ discuss the role social workers played in the group therapy program at the Boston State Hospital. Originally, psychiatric social workers were used as observers but gradually and increasingly they have been employed as group therapists. In many areas the social workers were admirably equipped for this type of therapy. However, in other areas, they needed greater training, particularly in the areas of intrapsychic dynamics and in recognizing and controlling their own blind spots and counter transferences. The authors' experience demonstrates that psychiatric social workers are capable of doing group therapy under the supervision of a psychiatrist. They also outline the kind of training and supervision that should be provided for beginning therapists.

Using Redl's formulations of different types of group formations, Klapman³⁵ finds that in actual practice, a mixture of the patriarchal, leader and tyrant type is encountered. Though individual and group therapy may overlap in some aspects, they do not exploit the same "segment of the psychotherapeutic spectrum. . . . Thus, group psychotherapy is no substitute for individual treatment." Group psychotherapy is seen as a catalyst, accelerating and facilitating individual therapy, and also, more than any other treatment method, as providing a milieu for a "living through" process.

GROUP PSYCHOTHERAPY WITH NON-PSYCHOTIC ADULTS

Durkin¹³ states that groups offer a particularly suitable milieu for the analysis of character traits. Habit patterns such as submissiveness, pseudo-aggression and over-politeness, when commented on or analyzed by the therapist, can uncover strong transference emotions and release previously repressed material. Treatment is thus maintained on a highly emotional level and the group accelerates the process by tracing the origin of traits. The author acknowledges that direct handling of defensive traits does create anxiety but this can be handled by the therapist.

The ego supportive values inherent in the group therapy situation with its opportunities for identification and group support are described by Woodward⁷⁰ as aids in a personality synthesis. Cases are cited in which marked improvement accrued within a brief period without real analysis of underlying dynamics. Insight into the mores of a particular group and understanding of a patient's defensive patterns in the group can be combined by the therapist to dissolve resistance. Fearing and McGregor¹⁵ describe such a therapeutic maneuver in which a patient is helped to add "group-relevant feeling" to his previously impersonal remarks.

Furst²² makes relevant observations on the relative advantages and disadvantages of diagnostically homogeneous and heterogeneous groups. Both types, it is stated, have their place in group therapy. Homogeneous groups seem more applicable where less profound treatment is indicated, where the therapist is not prepared to handle deep treatment levels and where factors of time and expense are important. The heterogeneous group, the author feels, is indicated where deeper levels of therapy and modification of character structure is sought.

Geller,²⁴ in discussing the size of therapy groups, advances the premise that depth of therapy decreases as size of the group increases. Thus, he believes that analytic groups can range from three to ten members while those concerned with guidance and orientation methods may be considerably larger.

From experience derived at Presbyterian Hospital in Philadelphia, Hadden²⁸ stresses the necessity of careful preparation in introducing the psychosomatic patient to group psychotherapy. The author describes that this patient has shopped around and is still seeking the right physician who will understand his case. A technic for accelerating group identification is given in having patients describe their symptoms at the initial session. The basic recognition is made that the group offers the opportunity of relieving in a positive way those experiences in the patient's life which have been traumatic for him.

Inability to express basic problems is cited by Ransberg⁵⁶ as the chief

criterion for selection of cases for individual therapy concurrent with group therapy.

Suggestions for exploitation of opportunities for group therapy in a pediatric hospital setting are made by Dubo.¹² The physician's informal contacts on the ward can be expanded into a group interview process; group therapy with children and parents in specific disease entities offers many potentials.

A group therapy experiment in a penal setting is described by Illing³² in which the release of hostility toward the worker and toward each other held positive meaning for the inmates. Work in a similar setting with female prisoners is reported by Fidler¹⁷ who found that a difficult obstacle was the suspicion toward the therapist as identified with administration. He also observes that a procedure centered on member interplay was more therapeutic than therapist-centered methods.

In observations on group therapy in a military hospital, Peck⁵¹ points out that group sessions were especially effective in measuring readiness to accept individual treatment. The author notes that initial suspicion toward authority was universal. In this setting, groups were permissive, met daily and were continuous. In working with combat breakdowns, the author notes that planning for a limited rehabilitary goal is often more realistic.

Boring and Deabler⁷ feel that of prime importance in conducting psychodrama is the securing of adequate and appropriate lifelike situations for the individual patient to participate in. The authors have simplified the problem by creating some twelve basic situations covering such situations as conflict between mother and son, father and son, divided loyalties, sibling rivalry, approaches to the opposite sex, job interviews, etc. These basic situations permit the patient to participate in more or less general roles and thus prepare him for participation in more personally structured ones related to his own conflict areas.

Simplified psychodrama is valuable to neuropsychiatric patients in that it enables them to share their private world with others. It helps them find their way back into normal social relationships and thus experience a sense of belonging. They can come face to face with their conflicts and, with the aid of the group, may resolve them. In many cases there is at least catharsis and abreaction if not full insight. In addition, patients have an opportunity in their role playing to test out new insights and new methods of adaptation. Furthermore, with the awareness that their problems are not unique, a greater self-acceptance and confidence develops which leads to more positive relationships with others.

Because of the resistances and initial anxieties presented by neuropsychiatric patients on admission to the hospital and the inability to deal

with this on an individual basis, an orientation program involving group discussion was instituted by Palmer.⁴⁹ Prior to the introduction of the orientation program patients were resistive to treatment, suspicious of psychotherapy, disciplinary problems, etc.

Group discussions were held twice weekly with an average attendance of 13 patients. Resident psychiatrists, nurses and attendants alternated in participation. After three months, the following changes were noted: (1) The whole ward was quieter during this period than any other times. (2) Patients were more observant of ward regulations, griped less and cooperation in work was increased. (3) Patients initially suspicious and hostile became interested in receiving psychotherapy. (4) Improvement in patient-staff relationships occurred.

Johnston³³ reports on an experiment with a group of voluntary male patients admitted to the hospital for treatment of drug addiction. Size of group varied from 9 to 14. Diagnostically the group consisted predominantly of character disorders, the largest grouping within this category being passive dependents. Cases were drawn from those deemed to have better prognoses than the general institutional population, an opinion based on age, duration of addiction and pre-addiction adjustment. In addition to the 12 weekly group sessions, each patient was also participating in the occupational therapy program and five were also in individual treatment.

The project was not aimed at effecting change in the basic personality structure of the narcotic addict. Rather, it was seen as an additional therapeutic element which would reenforce other therapies in the hospital and would help through intellectualization to strengthen superego resources. The results indicated that most of the group achieved a better understanding of the problem of drug addiction. Some members were stimulated to further interest as reflected in reading. Several achieved an understanding that their addiction was not a chance occurrence, but a personality problem requiring therapy.

Since behavior problems of children have their base in family relationships, Kahn, Buchmueller and Gildea³⁴ felt it was necessary to institute a group therapy program for parents of such children. The school was chosen as the most meaningful setting for this group operation since therapy can easily fit into the educational function of the school and thus save the parent from facing "badness," "delinquency," or "mental illness" necessitated by referral to a child guidance clinic or a court.

While group therapy programs in five all-white schools resulted in considerable success, a similar program in an all-Negro school met with failure. Basic reasons for failure of this program among Negroes seemed to lie "in minority tensions and status anxieties between group members which made

it impossible for the Negro mothers to face responsibility for their children. The behavior problems of their children could not be felt by them as clear-cut issues without contamination by ideas of discrimination."

Caplan¹⁰ reports that the combination of lecture and discussion technic is employed at the prenatal clinics in Jerusalem in order to prepare expectant mothers for childbirth and child rearing. Topics are selected in advance and are calculated to deal with the specific fears and anxieties of pregnancy and birth. Some of the topics are: mood swings during pregnancies, fantasies, fears and superstitions about the fetus, fear of dying during birth, difficulties with family during pregnancy, the approach to breast feeding, etc. Some of the subjects that the women themselves introduce are: fear of giving birth to monsters or deformed babies, fears of the evil eye, fear of having a big baby, sexual problems during pregnancy, household management, what to tell the other children about birth, etc.

In attempting to teach group dynamics to group therapists and observers at Boston State Hospital, Semrad and Arsenian^{5, 59} employed a group technic. Regardless of the way the group decided to study, so long as the leader maintained a non-authoritarian manner, there was true interaction and participation from the members. Habitual ways of getting along with other people, defense mechanisms, modes of handling anxiety and anxiety tolerance, all became apparent as the group progressed. The advantage of group methods of teaching lies in the display of reactions and interactions in a setting where one is alternately a participant and an observer.

Baruch and Miller⁶ employed paintings and drawings with a therapy group. Meetings were held weekly for an hour and a half in the therapist's home. The ensuing drawings were enthusiastically brought into the group where they evoked strong interest from the rest of the members, who immediately began to interpret the contents and the feelings of the artists. The therapist suggested that each member attempt to explore and explain what the picture meant to himself. Slides have also been used.

GROUP PSYCHOTHERAPY WITH NON-PSYCHOTIC ADOLESCENTS

In a paper dealing with the social re-education of delinquent young people, Slavson⁶⁰ indicates the satisfaction that is now voiced with the type of school that is at the present time attempting to re-integrate emotionally disturbed children into the community. He describes a procedure developed in a school of this nature in which the young people fully participated in the management of the reform school; he also emphasizes the importance of the "living group," in the cottage. In these groups, the most important influences are exerted in re-aligning the attitudes of the youngsters toward themselves and their environment. He also describes a program of creative expression and basic changes in the academic school. He further outlines

some difficulties in using group psychotherapy in a residential setting where the patients have contact with one another outside of the interview sessions, as well as the opportunities to reveal facts about one another to the total community.

Wollan⁶⁹ discusses the application of group therapy principles to institutional treatment of adolescents at the Connecticut Junior Republic. Here the peer group is viewed as a significant agent for remedial and therapeutic ends and is especially meaningful to the adolescent in that it does not challenge his basic antagonism to adult control.

Activity-interview group therapy with markedly deprived adolescent girls in a family agency setting is reported on by Stauffer.⁶⁶ After regression, members developed readiness to recognize motivation and were enabled to enter intensive individual treatment.

Grunwald, Headley et al.²⁷ present a thorough-going analysis of the group treatment of a 13-year-old Negro girl. This girl was not able to use individual treatment but did make excellent use of activity and discussion group therapy.

FOREIGN

The International Journal of Group Psychotherapy has also carried reports on group therapy activities in a number of countries. Among the contributors were Harding, Israel and Bernstein of Sweden,³⁰ Kraemer of England³⁶ and Rümke of Holland.⁶⁷ Hulse³¹ has also reported on the "International Aspects of Group Psychotherapy" which is a resumé of the papers and discussions on the subject at the First International Congress of Psychiatry in Paris.

GROUP PSYCHOTHERAPY WITH CHILDREN

In a paper on parallel treatment of children and their mothers, Fabian, et al.¹⁴ describe the relation of the treatment of a group of children five years of age and their mothers in a separate group. They find that "by virtue of interpatient identifications and an increased number of interpersonal relations it is possible to reach deeper layers in a shorter time than other therapies will allow." They also came to the conclusion that the "depth of treatment must be considered for the individual within the group as well as for the group as a whole, since the individuals do not function uniformly."

Lulow⁴⁰ reports on an experimental project in working with mothers of nursery school children as a prophylaxis against developing serious problems in children. This group of mothers met under the direction of a pediatrician-psychiatrist, to discuss some of the difficulties that the children presented in the home. The causes for these difficulties were explored and some of the attitudes of the patients analyzed. As a result, a number of

the mothers have come to the conclusion that they needed individual treatment for themselves, while the majority have modified their behavior. Lulow found that understanding the feelings of the mothers such as resentment, jealousy, love, hate, aggression and guilt have helped the mothers to deal with their children more constructively.

Dreikurs¹¹ discusses four types of group therapy employed in the Chicago Child Guidance Centers: (1) Family group—all members of the family are urged to participate in this group. The feeling is that the problems of the child express his interpersonal conflicts within the family rather than any intrapersonal conflict. With the family meeting as a group, interpersonal dynamics are exposed and explained to all the participants and new relationships are stimulated. (2) Children's group—in addition to Family Therapy, activity group therapy for children is also employed. This consists of free acting out plus psychodrama. (3) Parents' group—it seems that in this group only one family's problem is discussed at a time. The other parents act as sub-therapists until their problem is discussed at subsequent meetings. (4) Community's group—this group consists of visiting parents, teachers, social workers and others interested in children who represent the community. Their participation affects principles of education in the specific community agencies. The material presented is not of an intimate nature, the conflicts discussed deal more with interpersonal relationships that can be publicly divulged. (5) The Child in the Adult Group—in addition to the other forms of group therapy, a child will be interviewed in the presence of an adult group. The author feels that there are many advantages to this. He feels that the few minutes spent with the child in this situation seem to produce deeper and more constructive impressions than anything else that has been tried thus far.

Montague⁴⁸ describes the oral and anal regression of a nine-year-old boy in activity group therapy. During the therapy sessions, this boy acted out aggressively his anal-urethral interests by simulating elimination on a small pot in the presence of the other children, and at another session, he acted out his sexual fantasies by visualizing blood all around him and by crawling around on the floor pretending to lap up the blood with his tongue. He then proceeded to play out the cannibalistic ritual of the "king" eating his "subjects," the other boys of the group. The therapist converted the fantasy into reality by asking the boy: "Would your Majesty like a little milk?" The "king" appeared relieved, jumped up impulsively and joined the other children at the table. Montague proceeds to discuss the significance of this acting out in terms of the boy's problem with his mother by whom he was overprotected and overinfantilized. She also continues to describe how this boy had matured emotionally as a result of the treatment, how he had again and again tested reality and how his ego had been strength-

ened through this and the other influences of the therapeutic experience. Because of this the boy was able to accept limitations, assume the role of a more mature and strong leader in the group and became a much "happier boy."

Gersten²⁵ has experimented with effects of group therapy interview in an institution for juvenile delinquents. The subjects were 44 boys, 22 of whom were used as controls; 22 others were exposed to group interview sessions. The subjects were given a full battery of psychologic tests as well as ratings by staff members before the experiment was initiated. Spontaneous discussions were held as well as role playing for a period of 20 weekly sessions. Tests and evaluations were made of the subjects after the conclusion of the study. The recordings of the interviews were also evaluated independently by four members of the institutional staff: the psychiatrist, the director of social service, the case supervisor, and a group therapist of another training school—not the one who conducted the experiment. The subjects scored better than the controls in those categories that are considered indicative of better adjustment, such as M (human movement) responses, number of FC and CF (form-color), H (human) and P (popular) responses. The investigator came to the conclusion that group therapy sessions aided the boys in their social adjustment as compared with the youngsters in the control group. This was confirmed also by evaluations by the staff members of the institution.

Hallowitz²⁹ considered reports upon the use of group psychotherapy as preparation for individual treatment. After outlining the basic dynamic principles of activity group therapy, he shows the adequacy of this form of treatment for specific children with basic personality problems. Intensely neurotic children may not be able to accept individual treatment because of the difficulty in developing a transference relation and require a period of less demanding relations of an activity therapy group. He devotes a major part of his paper to the discussion of one ten-year-old boy who, though he needed intensive treatment, was not able to enter into a therapeutic relation and was helped to reach this stage through a period in activity group therapy.

Slavson⁶¹ discusses the role of authority, restraint and discipline in its dynamic relation to ego and superego development. He states that ego strengths can not be derived from verbal communication. Rather they develop through dynamic interaction and through active experiences with the world and people. The adult world errs considerably when it over-emphasizes external or direct discipline at the expense of furthering the development of self-restraint by slow stages through the desirable identifications and ego development. Repressive methods weaken the ego through inducing resentment and retarding emotional growth.

He presents illustrations of restraint as employed in therapy groups. In groups for pre-school children, it occurs mainly through interpretation. In addition to active restraint, passive restraint is employed as well, particularly in therapy groups. In fact the setting of a therapy room must be based upon the principle of passive restraint. By this he means the setting of a situational configuration that includes elements in the environment which in themselves condition the children's behavior. For example, windows should be so protected that there would be no danger of children falling against or through them; this obviates the necessity of the therapist constantly cautioning the children against danger. Other examples are also offered.

"It is in identifying with the positive characteristics of the therapist that foundations for the ego strengths and super-ego development in children are laid. Emotional growth occurs indirectly, automatically, as a response to a satisfying relation with an adult rather than in direct prohibition and restraint that tend to arouse hostility and cause regression."

Meals and Summerskill⁴⁶ confronted with the problem of dealing with the extreme hostility displayed by boys in a group situation, constructed a target consisting of a large plywood board (36" x 54") with an eight-inch-diameter hole near the bottom. Over this opening pictures were fastened by scotch tape so that bean bags thrown at the target could strike and destroy the picture. The children made their own pictures, for example, a man, a woman, a school teacher, etc. This technic was successful in diverting the hostility away from weaker, more passive children and it also "afforded valuable opportunities for the therapist to recognize, accept and reflect feelings and problems which came to light. . . ."

The application of some aspects of group therapy to classroom practice according to Maas⁴¹ follows a three-stage sequence: (1) the primary school (2) the intermediate grades through early junior high school, and (3) junior and senior high schools and the college years.

REFERENCES

- ¹⁻⁴ Internat. J. Group Psychotherapy. Volume I, Numbers 1-4, 1951.*
- ⁵ Arsenian, John and Semrad, Elvin: Application of analytic observation to teaching group dynamics. *J. Psychiat. Soc. Work.* 20:150, 1951.
- ⁶ Baruch, Dorothy and Miller, Hyman: The use of spontaneous drawings in group therapy. *Am. J. Psychotherapy.* 5:45, 1951.
- ⁷ Boring, R. O. and Deabler, H. L.: A simplified psychodramatic approach in group therapy. *J. Clin. Psychol.* 7:371, 1951.
- ⁸ Breckir, Nathaniel J.: Group psychotherapy with psychotic patients. *Internat. J. Group Psychotherapy.* 2:129, 1951.

* All references to Internat. J. Group Psychotherapy refer to Vol. I. The first numeral in these references (in italic) applies to the number of the issue in Vol. I.

- ⁹ Bry, Thea: Varieties of resistance in group psychotherapy. *Internat. J. Group Psychotherapy*. 2:106, 1951.
- ¹⁰ Caplan, Gerald: Mental hygiene work with expectant mothers. A group psychotherapeutic technique. *Ment. Hyg.* 35:41, 1951.
- ¹¹ Dreikurs, Rudolf: Family group therapy in the Chicago community child guidance centers. *Ment. Hyg.* 35:291, 1951.
- ¹² Dubo, Sara: Opportunities for group therapy in a pediatric service. *Internat. J. Group Psychotherapy*. 3:235, 1951.
- ¹³ Durkin, Helen E.: The analysis of character traits in group therapy. *Internat. J. Group Psychotherapy*. 2:133, 1951.
- ¹⁴ Fabian, Abraham A., Crampton, Jessie E., and Holden, Marjorie, A.: Parallel group treatment of pre-school children and their mothers. *Internat. J. Group Psychotherapy*. 1:37, 1951.
- ¹⁵ Fearing, John M. and McGregor, Robert: Analysis of the group process in the therapeutic session. *Internat. J. Group Psychotherapy*. 2:126, 1951.
- ¹⁶ Fidler, Jay W., Jr.: The concept of levels in group therapy with psychotics. *Internat. J. Group Psychotherapy*. 1:51, 1951.
- ¹⁷ —: Possibilities of group therapy with female offenders. *Internat. J. Group Psychotherapy*. 4:330, 1951.
- ¹⁸ Foulkes, S. H.: Concerning leadership in group-analytic psychotherapy. *Internat. J. Group Psychotherapy*. 4:319, 1951.
- ¹⁹ —: Group therapy. *Brit. J. M. Psychol.* 23:199, 1950.
- ²⁰ Frank, Jerome D. and Ascher, Edward: Corrective emotional experiences in group therapy. *Am. J. Psychiat.* 108:126, 1951.
- ²¹ Frank, Jerome D.: Some problems of research in group psychotherapy. *Internat. J. Group Psychotherapy*. 1:78, 1951.
- ²² Furst, William: Homogeneous versus heterogeneous groups. *Internat. J. Group Psychotherapy*. 2:120, 1951.
- ²³ Gabriel, Betty: Analytic group psychotherapy with a borderline psychotic woman. *Internat. J. Group Psychotherapy*. 3:243, 1951.
- ²⁴ Geller, Joseph J.: Concerning the size of therapy groups. *Internat. J. Group Psychotherapy*. 2:118, 1951.
- ²⁵ Gersten, Charles: An experimental evaluation of group therapy with juvenile delinquents. *Internat. J. Group Psychotherapy*. 4:311, 1951.
- ²⁶ Glenn, Jules: Values of group discussions with psychiatric aides in a mental hospital. *Internat. J. Group Psychotherapy*. 3:254, 1951.
- ²⁷ Grunwald, Hanna, Headley, Dorothy, Stevens, Rutherford B., Slavson, S. R., Thompson, Jean A., and Neubauer, Peter: The case of Jean Case. *Internat. J. Group Psychotherapy*. 1:64, 1951; 2:154, 1951.
- ²⁸ Hadden, Samuel B.: Group psychotherapy in general hospitals. *Internat. J. Group Psychotherapy*. 1:31, 1951.
- ²⁹ Hallowitz, Emanuel: Activity group psychotherapy as preparation for individual treatment. *Internat. J. Group Psychotherapy*. 4:337, 1951.
- ³⁰ Harding, Gusta T., Israel, Joachim, and Bernstein, Lotte: Group therapy in Sweden. *Internat. J. Group Psychotherapy*. 1:82, 1951.
- ³¹ Hulse, Wilfred C.: International aspects of group psychotherapy. *Internat. J. Group Psychotherapy*. 2:172, 1951.
- ³² Illing, Hans A.: The prisoner in his group. *Internat. J. Group Psychotherapy*. 3:264, 1951.
- ³³ Johnston, McClain: An experiment in group psychotherapy with the narcotic addict. *Am. J. Psychotherapy*. 5:24, 1951.

- ³⁴ Kahn, Jane, Buchmueller, A. D., and Gildea, Margaret, C. L.: Group therapy for parents of behavior problem children in public schools. *Am. J. Psychiat.* 108:351, 1951.
- ³⁵ Klapman, J. W.: Clinical practices of group psychotherapy with psychotics. *Internat. J. Group Psychotherapy.* 1:22, 1951.
- ³⁶ Kraemer, W. P.: Group psychotherapy at the Davidson Clinic, Edinburgh, Scotland. *Internat. J. Group Psychotherapy.* 3:281, 1951.
- ³⁷ Kusch, Ernest H. and Lucas, Leon: Group guidance in preparation for convalescent care. *Psychiat. Quart. Suppl.* 23:245, 1949.
- ³⁸ Lawton, James J. Jr.: The expanding horizon of group psychotherapy in schizophrenic convalescence. *Internat. J. Group Psychotherapy.* 3:218, 1951.
- ³⁹ Luchins, Abraham S.: Restructuring social perceptions: A group psychotherapy technique. *J. Consult. Psychol.* 14:446, 1950.
- ⁴⁰ Lulow, William V.: Disorders in a group of nursery school children. *Internat. J. Group Psychotherapy.* 2:144, 1951.
- ⁴¹ Maas, Henry S.: Applying group therapy to classroom practice. *Ment. Hyg.* 35:250, 1951.
- ⁴² Mann, James: An analytically oriented study of groups. *J. Psychiat. Soc. Work.* 20:137, 1951.
- ⁴³ McCann, Willie H. and Almada, Albert A.: Round table psychotherapy: A technique in group psychotherapy. *J. Consult. Psychol.* 14:421, 1950.
- ⁴⁴ McDonald, Eugene C.: The masking function of self-revelation in group therapy. *Internat. J. Group Psychotherapy.* 1:59, 1951.
- ⁴⁵ Mead, Margaret: Group psychotherapy in the light of social anthropology. *Internat. J. Group Psychotherapy.* 3:193, 1951.
- ⁴⁶ Meals, Donald W. and Summerskill, John: A technique for dealing with hostility in activity therapy. *J. Clin. Psychol.* 7:376, 1951.
- ⁴⁷ Menzer, Doris, Irvine, Lillian S., and Semrad, Elvin: The role of the social worker in group therapy. *J. Psychiat. Soc. Work.* 20:158, 1951.
- ⁴⁸ Montague, Harriet Cary: A case of regression in activity group therapy. *Internat. J. Group Psychotherapy.* 3:225, 1951.
- ⁴⁹ Palmer, James O.: Group discussions as a method of patient orientation in a neuropsychiatric hospital. *J. Clin. Psychol.* 6:369, 1950.
- ⁵⁰ Peck, Harris B.: Group psychotherapy and mental health. *Internat. J. Group Psychotherapy.* 4:301, 1951.
- ⁵¹ Peck, Robert E.: Observations of group therapy in an army general hospital. *Internat. J. Group Psychotherapy.* 4:365, 1951.
- ⁵² Powdermaker, Florence B.: Psychoanalytic concepts in group Psychotherapy. *Internat. J. Group Psychotherapy.* 1:16, 1951.
- ⁵³ Powell, John W.: The dynamics of group formation. *Psychiatry.* 11:117, 1948.
- ⁵⁴ Prados, Miguel: The use of films in psychotherapy. *Am. J. Orthopsychiat.* 21:36, 1951.
- ⁵⁵ —: The use of pictorial images in group therapy. *Am. J. Psychotherapy.* 5:196, 1951.
- ⁵⁶ Ransberg, Mary: Integration of group therapy and individual therapy. *Internat. J. Group Psychotherapy.* 2:115, 1951.
- ⁵⁷ Rumke, H. C.: Group psychotherapy in Utrecht, Holland. *Internat. J. Group Psychotherapy.* 4:374, 1951.
- ⁵⁸ Schindler, Walter: Family pattern in group formation and therapy. *Internat. J. Group Psychotherapy.* 2:100, 1951.

- ⁵⁹ Semrad, Elvin and Arsenian, John: The use of group processes in teaching dynamics. *Am. J. Psychiat.* 108:358, 1951.
- ⁶⁰ Slavson, S. R.: Social re-education in an institutional setting. *In* *Advances in Understanding the Offender*. New York, National Probation and Parole Association, 1950.
- ⁶¹ —: Authority, restraint and discipline in group therapy with children. *Nerv. Child.* 9:187, 1951.
- ⁶² —: Catharsis in group psychotherapy. *The Psychoanalyt. Rev.* 38:39, 1951.
- ⁶³ —: Current trends in group psychotherapy. *Internat. J. Group Psychotherapy.* 1:7, 1951.
- ⁶⁴ —: The dynamics of analytic group psychotherapy. *Internat. J. Group Psychotherapy.* 3:208, 1951.
- ⁶⁵ Standish, Christopher T. and Semrad, Elvin V.: Group psychotherapy with psychotics. *J. Psychiat. Soc. Work.* 20:143, 1951.
- ⁶⁶ Stauffer, Marjorie: Group psychotherapy in a family agency. *Internat. J. Group Psychotherapy.* 4:348, 1951.
- ⁶⁷ Wender, Louis: Current trends in group psychotherapy. *Am. J. Psychotherapy.* 5:381, 1951.
- ⁶⁸ —: Selection of patients for group psychotherapy. *Internat. J. Group Psychotherapy.* 1:55, 1951.
- ⁶⁹ Wollan, Kenneth I.: Application of group therapy principles to institutional treatment of adolescents. *Internat. J. Group Psychotherapy.* 4:356, 1951.
- ⁷⁰ Woodward, Walter: Spontaneous personality synthesis in group therapy. *Internat. Group Psychotherapy.* 2:123, 1951.

Shock Therapy*

By PAUL H. WILCOX, M.D. AND ILSE ADLER

INTRODUCTION

TWO TEXTBOOKS on therapy appeared in German.^{14, 90} Wortis²³⁴ reviewed the treatment theories and practice in Soviet Russia. Steinfeld²⁰⁶ published a monograph on therapy for psychotics, stressing the electroshock and psychotherapy aspects. Wortis²³³ and Levy¹²⁰ reviewed 1950 progress in psychiatric therapy.

Stockings²¹² attempts to distinguish two types of deranged cerebral oxygen-glucose metabolism on the basis of their response to convulsive ("anoxic") vs. hypoglycemic therapy. Although in one type depressive features are often prominent some of the acute schizophrenias respond similarly. He, therefore, considers the test of therapy more important in determining the final diagnosis than the clinical symptoms alone.

INSULIN THERAPY

Insulin Coma Therapy (ICT)

Indications. Many experienced clinicians reiterate that ICT is the treatment of choice for most schizophrenics, adding supplementary ECT—or ECT during ICT—for the affective components and in resistant cases.^{51, 65, 106, 129, 135, 162, 167, 168, 187} To date, no tests have been found which give a reliable indication to the effect that any patient will do poorly with psychotherapy alone or with electroconvulsive therapy alone, but will respond well to insulin coma therapy. However, there is a persistent clinical impression that ICT does work in some cases when the other treatments have failed, but this can only be found by trial and error.

Gottlieb and Huston⁷⁵ in three carefully matched series of schizophrenics did not find any significant difference in the clinical status over a one to

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four year follow-up period between early schizophrenics treated with brief psychotherapy alone, ECT alone or ICT alone. Short duration of illness before the start of treatment improved the prognosis with each of the three methods. The subtypes differed from one another in their response to treatment but not as to type of treatment. The recovery rates for all three treatment groups when combined were: simple, 23 per cent; hebephrenic, 28 per cent; paranoid, 40 per cent; and catatonic, 47 per cent. Cohen⁴⁴ failed to discover any prognostic factor other than the general one of duration of illness. More reliable prognostic evidence may come from the work of Funkenstein et al.⁶⁴ who reported that cases in whom anxiety is precipitated by a standard test dose of epinephrine (0.05 mg. I.V.) respond to ICT but are aggravated by ECT. Another group of patients in whom there is an elevation of the basal BP, and the epinephrine test does not produce anxiety, and mechloryl (10 mg. I.M.) produces only slight and transient fall in BP, respond poorly to ECT but about 50 per cent of them respond to ICT. These patients seem to be suffering from a hypersecretion of nor-epinephrine.^{62, 63, 133}

Juvenile schizophrenia tends to have a poor prognosis with ICT as well as with ECT.^{42, 121}

Neurophysiology and Biochemistry. Himwich⁸⁶ has contributed greatly to our understanding of the symptoms of hypoglycemic coma on the basis of the phyletic organization of the central nervous system. Five phases can be distinguished, namely (1) the cortical phase, (2) the cortico-diencephalic phase, (3) the mesencephalic phase, (4) the premyelencephalic phase, and (5) the myelencephalic phase. As deep coma is approached, successive phyletic layers are released from the controls of the higher layers. When the patient is brought out of coma this process is reversed step by step. The reason for this sequence seems to be that the higher phyletic levels operate at successively higher metabolic rates and, therefore, suffer in the order of the higher to the lower when subjected to loss of fuel. The blood sugar levels do not correlate with the clinical symptoms except during the first phase, but the EEG changes do. There is a close parallel between the progressive stages of hypoglycemic coma and of anoxic anoxia produced by nitrogen inhalation. It thus appears that in ICT there is a progressive dampening of the brain oxidations. It must be further understood that there are two main components of the metabolism of brain cells. One maintains cell integrity and the other supports the functional activity of the neurone discharges. This explains how the neurones can become non-functional but still revive when normal metabolic conditions are restored. However, in the case of protracted coma the maintenance limits are severely taxed, and the restoration is very slow but still actually follows

step by step the phyletic recapitulation pattern of the uncomplicated emergence from insulin coma, sometimes stretched over a period of several days.

Pflugfelder¹⁵⁷ claimed not to be able to demonstrate the dissolution of function in reverse phylogenetic order. He distinguished three types of hypoglycemic reactions in the first stage: (1) excitation and motor hyperkinesis, (2) drowsiness without dramatic phenomena and (3) akinesis and mutism. These reactions seem more correlated to personality than to type of psychosis. He defines onset of coma as occurring when there is no longer any reaction to pain on maximal pinching of the skin and muscle tissue in the area of the posterior wall of the axilla. The loss of the palpebral reflex occurs slightly before "coma" is reached. The loss of the corneal reflex tested with a wisp of cotton marks the onset of "deep coma" and is his indication for the immediate interruption of the hypoglycemia.

Cossa and Martin⁴⁶ point out that those patients who show marked grimaces and myoclonic jerks in the second phase of ICT show predominance of slow EEG waves in the temporal regions. They raise the question of whether ICT acts selectively on the temporal lobes. Weinland and Weinland²²⁴ describe a gradual shift in the EEG during the stages of insulin hypoglycemia consisting of a decrease in frequency and increase in amplitude to an amorphous picture in deep coma. Jung⁹⁹ also reports a slowing of the brain waves during ICT, and in some cases this persists at least for a time after a course of ICT.⁶¹

Tsai et al.²¹⁸ outline the progression of hormone influences following insulin hypoglycemia as (1) liberation of epinephrine which in turn (2) liberates ACTH which (3) activates the adrenal cortex resulting in (4) a fall in the circulating eosinophiles and lymphocytes. However, Vogt²²³ demonstrated in rats that insulin hypoglycemia evoked ACTH even after removal of the adrenal medullae. Probably ICT is safer than ECT in patients having glaucoma because deep insulin coma produces little or no increase in intraocular pressure but ECT does.¹³⁷ Bonparis³¹ supports the French opinion that amorphous insulin is more beneficial and less hazardous than purified insulin in ICT.

Complications and Neuropathology. The therapist should be on the alert for the complications which may arise during the ICT. Billet et al.²⁸ list the following complications of ICT: spasms of the glottis (dangerous but rare), acute edema of the limbs, hemiplegia, hemiparesis, aphasia, epileptic seizures, pulmonary gangrene and protracted coma. They theorize that the therapeutic action of ICT may be due to "disintoxication" of the nervous centers during cerebral edema. However, if the cerebral edema becomes excessive it tends to cause protracted coma. They give rapid I.V. injections of 10 to 20 cc. of chilled 15 per cent magnesium sulfate solution

as soon as any signs of neurologic disturbance persist for 15 minutes. They have thus for three months avoided protracted comas. Meyers and Shurley¹⁴² report using Rivers and Rome's method of dealing with protracted comas since 1944 in 116 instances. Recovery in less than 2 hours occurred in 87 per cent of the occasions and there were no fatalities. ICT was not discontinued in any of the cases because of the protracted coma. Abély (in Bergeron and Chertok²⁴) discussed the possible bearing of Selye's general adaptation syndrome on protracted comas. In some cases there is an exhausted adrenal cortex resulting in insulin hypersensitivity and in others a hyperplastic adrenal cortex producing insulin resistance. For the first cortisone is indicated and for the second, its antagonist, desoxycorticosterone. Acute pulmonary edema may complicate ICT and if it is detected early and promptly treated with bronchoscopic aspiration (when indicated), oxygen tent, digitalis, coramine and antibiotics, good recovery occurs.⁴³ Halle and Ross⁷⁸ report transitory reversible neurologic complications of ICT such as paresis of one arm or one side of the face, or aphasia lasting 2 to 48 hours. Hemiplegia has been reported.³⁰ Residual mental impairment sometimes follows a successfully treated protracted coma.⁶⁶ Even slight temperature elevation calls for immediate termination of the coma^{6, 43} because of the greatly increased threat of brain damage as reported by Tyler in 1941.²¹⁹ Russek et al.¹⁸⁰ consider insulin coma convulsions as complications and recommend 6 grains of papaverine orally 45 minutes before the usual injection of insulin. Dahl⁴⁹ reports that occasionally women develop a general allergy reaction to insulin when given successive courses of ICT. Kersley et al.¹¹¹ suggest a high protein diet and evening snacks for three weeks following a course of insulin therapy to prevent the occasional complication of spontaneous hypoglycemia.

Donnelly and Radley-Smith⁵⁴ describe a "hydrocephalus" due to a partial thrombosis of the superior longitudinal sinus during ICT, which results in a moderate increased CSF pressure without other changes in the CSF. The treatment was repeated removal of small amounts of CSF by lumbar puncture.

Lorentzen¹²⁷ used the gallocyanin-chromalum staining method to study the cortical cell changes during various stages of insulin coma in experimental animals and found that some nerve cells, especially in the fifth layer, became chromophobic during the coma. Some of these apparently resynthesized their nucleoproteins after treatment while others degenerated into cell shadows.

Technic. Shurley¹⁹⁵ stresses the lack of adequate training centers for ICT which is a difficult and dangerous therapy. Robinson¹⁷⁵ reports good results with the rapid induction method. Mewhort¹³⁹ published some very practical suggestions for an insulin therapy cart.

Yagdjoglou²³⁵ recommends dividing the insulin dose and injecting it into two or more parts of the body. He claims this requires less insulin and less glucose for arousal.

Psychodynamics. Arikian¹² emphasizes that the depth of the insulin coma treatment should be individualized because the patients' reactions vary from day to day. The depth and duration of the coma should be regulated by trial and error to find the most desirable clinical response. Levy¹¹⁹ recommends giving I.V. sodium amytal for narcosynthesis as soon as the patient begins to respond after termination of coma. A follow-up interview the same afternoon is used to develop insight into the material elicited in the morning. He claims that by this procedure the required time for the ICT was reduced from an average of 13 weeks to 6 to 8 weeks.

Insulin comas may be dramatized as death experiences, as reported in two schizophrenics who had failed to be benefited by ICT and subsequently improved under psychoanalysis.^{81, 138}

Psychologic Studies. In his analysis of the alterations of consciousness during insulin therapy, Pflugfelder¹⁵⁷ studied the stages of drowsiness by means of hand writing, counting of dot figures, naming of pictures and objects, the slowing of perception, object assembly, slowing on a numbers table and serial sevens, and concluded that hypoglycemia leads to a qualitative change of consciousness in the sense of an organic clouding of consciousness which is unlike physiologic sleep. He suggests that the break in the continuity of experiencing life is a factor in the therapeutic process.

The psychologic literature over the past ten years has been reviewed by Lipton et al.¹²⁶ for evidence on the changes in schizophrenics undergoing Sakel's treatment, most of this evidence based on the Wechsler-Bellevue and the Rorschach tests. From these sources, a series of 15 signs has been culled and applied to the Rorschach records of 15 paranoid schizophrenics without knowledge of psychiatric ratings, and they proved of value in making prognostic estimates of improvement under ICT. The positive signs on the Rorschach were: (1) productivity of more than 25 responses; (2) a color sum of 2.5 or greater; (3) a percentage of good form response of 70 or greater; (4) the presence of one or more good human movement responses; (5) the presence of 3 or more sharply perceived whole responses. The negative signs were: (1) three or more rejections on the Rorschach; (2) a Wechsler-Bellevue I.Q. of less than 90. However, no psychological signs have been demonstrated to mean that the prognosis is better with ICT than with ECT.¹⁵⁶

Miscellaneous Insulin Procedures

Rackow¹⁶⁵ reported that subcoma insulin and psychodrama produced improvement in the hospitalized patients with anxiety symptoms but most

of those discharged relapsed within 3 to 16 weeks. Subcoma insulin is usually ineffective in obsessional neuroses.¹⁸⁸ Subcoma insulin is being tried in the treatment of rheumatoid arthritis with moderate success.^{74, 110} Van Amberg²²¹ claims that subcoma insulin is valuable in office practice for the anxiety neuroses characterized by tension, depletion, over-excitation and g-i disturbances but is ineffective for phobias and panics.

The combination of cortisone and ICT has so far yielded inconclusive results.¹²² Sackler et al.^{181, 182} and De⁵² have tried histamine with subcoma insulin therapy in schizophrenia.

Palmer and Garrett¹⁵² treated 30 cases of chronic schizophrenia (average duration before start of treatment 18 months, range 4 to 68 months) with a full course of ICT followed by 20 ECT with only temporary improvement in most cases.

METRAZOL THERAPY

Metrazol convulsive therapy (MCT) continues to be largely replaced by electroshock convulsive therapy (ECT), but Dax⁵¹ recommends MCT for feeding difficulties, stupor, depression with marked delusions, mania with much psychomotor activity and certain cases of schizophrenia which have failed on other therapies. He reports less memory defects after MCT than after ECT but states that tb is more easily reactivated and more fractures occur with MCT. Karliner¹⁰⁶ suggests 1 to 2 cc. of 10 per cent metrazol I.V. immediately prior to ECT in patients with a high convulsive threshold and claims the tendency to prolonged apnea is diminished by this procedure.

For inducing convulsions during insulin coma some authors still prefer metrazol.^{92, 106} Kajtor^{101, 102} prevented metrazol but not electric seizures with histamine.

Although subconvulsive metrazol treatments have been considered ineffective in endogenous depressions, Kraemer¹¹⁵ recommends small doses (av. 2 cc., max. 3 cc.) given I.V. rapidly for some mixed and reactive depressions, daily at the start and also as an auxiliary or follow-up treatment in conjunction with convulsive therapy. These treatments do not interrupt consciousness, but produce transient reactions, viz: dizziness, flickering sensations, slight tremors, smile, blushing, slight shudder and slight cough and in some cases a more prolonged floating feeling. Unexpectedly, some transient memory disturbances were observed even though consciousness was not interrupted.

O'Flanagan et al.¹⁴⁹ report further observations on subconvulsive treatment with combined hexazol (triazol) and photic stimulation. The dose is adjusted so that no clinical or EEG changes occur with the hexazol alone, but EEG dysrhythmia and myoclonic twitches appear with the addition

of stimulation by bright flashes (10 to 30 per sec.) applied close to the patient's closed eyes. The treatment is continued for 5 to 10 minutes and induces a number of vivid subjective experiences. The indications for this technic have not yet been clearly formulated.

ELECTRICAL STIMULATION

Barhash¹⁶ writes: "I am one among those who feel that many psychiatrists resort to electroshock treatment too quickly, too frequently and too exclusively. It is very useful in severe depression, especially where the threat of suicide makes quick treatment imperative, or where other forms of treatment such as psychotherapy have already proved ineffective." However, it will be apparent from this review that "electroshock treatment" is not a single modality, but now has developed into a complexity of technics requiring broad training and experience in order to select what is best suited for any particular patient.

Technical Considerations

Introduction. The reader is referred to Volumes II and VI of this series for comparisons between the Cerletti-Bini (classical) ECT, the Delmas-Marsalet technic, the Friedman-Wilcox-Reiter technic (old Reiter), the new series of Reiter Electrostimulators (CW 46J, CW 47, and RC 47), the Liberson Brief Stimuli technic (B.S.T.), the Tietz Electronarcosis (E.N.), Olsen and Dale 10 to 30 sec. technic, and combined ICT and ECT and other variations. General discussion and description of ECT technics are included in several references.^{8, 14, 36, 56, 68, 80, 92, 106, 132}

v. Braunmühl⁸⁵ describes a new ECT instrument delivering interrupted unidirectional pulses, being a compromise between the old Reiter and the Liberson currents. Jannuccelli⁹⁷ reports encouraging results in treating enuresis in mental defectives and epileptics with lumbar-pubic electroshock.

Stimulation Patterns. Wilcox²²⁹ outlined four treatment levels following Reiter's recommendations which can be summarized as low non-convulsive electrostimulation (low E.S.mc.), high non-convulsive electrostimulation (high E.S.nc.), low electroconvulsive treatment (low ECT) and high electroconvulsive treatment (high ECT) using a rheobase convulsive stimulation as the dividing line. Thus a high E.S.nc. is below, but near the rheobase convulsive level and a low ECT is above but also near the rheobase level.

Hirschfeld and Bell⁸⁷ using a brief stimuli square wave current (Liberson) with variable peak, pulse duration and frequency have described what they call four stages of differential cerebral stimulation. Their technics

are not identical with the four levels of stimulation Wilcox described, but the first two "stages" are subconvulsive and the second two are convulsive.

The place of non-convulsive cerebral electrostimulation is receiving increasing attention not as a substitute for ECT's but in cases which respond poorly to ECT. Plattner and Löhnis¹⁵⁹ did some early work in this field, recommending subconvulsive electrostimulation for the treatment of arteriosclerotic and senile depressions, using phenobarbital orally as premedication. Berkwitz²⁵ has followed up his early work with non-convulsive faradic stimulation and now uses 0.25 gm. sodium amytal, I.V. as routine premedication. He finds this technic useful in neurotic depressions, obsessive-compulsive states, conversion hysteria and in some types of psychosomatic disorders. Impastato⁹³ proposes a method of giving sodium pentothal (thiopental sodium) safely as a premedication for non-convulsive Reiter electrostimulation. The I.V. injection of 5 per cent aqueous solution of sodium pentothal is begun slowly while the electrodes are held in place in the temporo-parietal region. During the injection small test stimulations are given and when the patient first can take 2 ma. of the Reiter CW 47 No. 1 current without moving the hands, the optimum amount of sodium pentothal has been injected and the full non-convulsive stimulation can proceed. This avoids an overdosage of sodium pentothal but ensures enough so that the desired stimulation can be carried out without causing the patient discomfort. This technic can be adapted to other currents by determining for each current what strength meets the above specifications.

Larragoiti¹¹⁶ reports favorable experience with low E.S.nc. Milligan¹⁴⁶ reports a 15 minute non-convulsive technic using sodium pentothal anesthesia, d-tubocurarine, carbogen inhalation and 85 ma. of 60 cycle a.c. This can be classified as a low E.S.nc. technic. He reports benefits in depressions and in paranoid schizophrenics. This indicates the need to define depressions exactly because other reports indicate that E.S.nc. tends to make endogenous depressions worse but may help reactive depressions.

Impastato⁶⁰ has been using the continuation of above rheobase strength of current during the clonic phase as a modified Reiter technic since 1948. Alexander^{1, 2} has described this modified Reiter technic in detail. After the convulsive stimulus has induced the onset of the tonic phase of the convulsion, the current is maintained at a level which somewhat softens the tonic pull and splints the clonic phase. Towards the end of the clonic phase, 30 to 50 seconds after the start of stimulation, the current is reduced enough to let a faint trace of the clonic phase come through so the end of the clonic phase can be observed, and then the current is reduced to a low level but left on as a respiratory stimulus till respirations are resumed. The modulated Reiter current works well for respiratory stimulation but it must

always be remembered that the strength of this stimulation must be individually determined, because if it is too strong, respiration continues to be inhibited. This electrical suppression of the clonic phase does not decrease the anti-depressant effect of the treatment but does decrease the fracture hazard so that the convulsion-softening drugs are very rarely necessary.

Electronarcosis (E.N.) is compared to other electroshock methods in several reports.^{5, 39, 45, 164, 217} Wilson²³² describes an instrument which delivers pulses of only 5 microseconds duration, frequency 80 per second and pulse peaks up to 1,250 volts for giving E.N.

Brussel and Schneider³⁸ report "blitz electric shock therapy" (B.E.S.T.) for chronic disturbed patients, 600 ma. 60 cycle a.c. for 0.5 seconds being given each morning and afternoon of two successive days. This produced a marked improvement of ward behavior and was repeated whenever the patient showed the prodromata of relapse.

Koenig and Feldman¹¹³ recommend what they call "double treatments" daily for chronic disturbed patients till ward behavior has improved. A "double treatment" is two standard ECT's separated by 1½ hours. Neither of these intensive technics is "regressive" because ward improvement is the signal for interrupting the series. However, Rothschild et al.¹⁷⁷ attempted to treat 52 patients with 28 ECT's in 7 days, giving 2 each morning separated by 1 to 2 hours and two similarly each afternoon. A few of the patients did not receive the full number, but the patients all showed a profound organic confusion reaction with double incontinence and retardation. Recovery from the organic reaction was gradual. The ability to walk, feed oneself, talk and be continent usually was reestablished by the end of the first post-treatment week and some interest in personal appearance developed during the second week. The authors did not observe permanent ill effects but considered it a drastic procedure to be reserved for those patients who have failed to respond to the more standard treatment schedules. Of the 52 patients, 5 made a social recovery and 22 were unimproved. The rest showed various degrees of improved ward adjustment.

Stengel²⁰⁷ tried a similar pattern of "annihilation therapy" on ten severe chronic hysterical and obsessional psychoneurotics and reported serious retrograde amnesia which persisted for months and years in some cases, and only three of his cases showed much improvement.

Singh²⁰⁰ reported improved results by giving daily "intensified ECT's." Each treatment consisted of the initial convulsive stimulus and rapidly repeated similar stimuli during the tonic and clonic phases, sometimes as many as 13 such stimulations being given in one convulsion. Steinfeld²⁰⁵ recommends multiple ECT's in patients who failed to respond to single or double ECT's and follows with some sub-shock electrostimulations to

reduce the confusional after-effects of the intensive ECT's. Stevenson and Geoghegan^{209, 210} continue to report success with prevention of recurrent manic attacks by regular prophylactic ECT, usually only one a month being necessary.

Frosch et al.⁶⁰ report the rapid treatment of depressions with the Reiter currents giving two ECT's the first day and then one daily till improvement appears and then spacing the treatments. This degree of intensification of treatment schedule with the Reiter currents seldom produces any hangover mental confusion and usually results in dramatic relief in a few days. McCartney¹³⁶ also reports less post-treatment amnesia and confusion with Reiter ECT's than with the Cerletti-Bini technic.

Combined Treatments. Sackler et al.¹⁸² recommended a trial four week course of histamine therapy in various psychoses, and for some of those patients who fail to respond, histamine and ECT combined. In the latter technic, atropine sulfate gr. 1/150 to 1/100 is injected subcutaneously at the same time as the second histamine dose. Approximately 30 minutes later, at the end of the histamine reaction, a 2.5 per cent solution of thiopental sodium is given I.V. slowly till the lid reflex is absent and then ECT is given. They observed less post-convulsive confusion with this combination than with ECT alone.

Modifying Drugs. Numerous articles detailing the advantages and disadvantages of various curare-like drugs for softening therapeutic convulsions continued to appear in the literature, but the summary given in Volume VI of this series²²⁹ does not need modification at this time. Thompson and Norton²¹⁵ consider that gallamine triethiodide (flaxedil) is superior to d-tubocurarine and to C-10 in modifying ECT in most cases. However, they prefer C-10 in asthmatics. They give the flaxedil (60 to 80 mg.) mixed with atropine gr. 1/100 and thiopentone 0.25 Gm. in one syringe by rapid I.V. injection 90 seconds before the convulsion and 1 cc. (1 mg.) of neostigmine I.V. right after the convulsion. Silfverskiöld¹⁹⁶ recommends giving neostigmine (1 mg. in 1 cc. I.V.) after the curare before the convulsion but holding it in the vein by a pressure cuff inflated to 250 mg. Hg. until the clonic phase has started at which time the pressure is released, so the neostigmine enters the circulation.

Rowe et al.¹⁷⁸ believe that most patients with cardiac disease can tolerate ECT if they are given curarization and atropinization before each treatment. They administer oxygen after the convulsion and have neostigmine, cardiac medication and an intratracheal tube available if needed.

Korson¹¹⁴ reported using spinal anesthesia preceded by 0.5 cc. neosynephrine in order to give ECT safely to a man with a recent fracture of the femur.

Kerman¹⁰⁹ found that in 90 per cent of patients who show nausea fol-

lowing ECT, the nausea can be prevented by 100 mg. of dramamine given one hour before each subsequent ECT. McCartney¹³⁶ confirms this observation.

Place of Treatment. Impastato et al.⁹⁴ describe the advantages of the Reiter ECT's in office and out-patient practice, especially because of the minimal memory disturbances. Gayle⁶⁷ recommends that general hospitals should offer facilities for the administration of the various shock therapies but advises that ECT be given only to those out-patients who have first been treated as in-patients. Fetterman et al.⁵⁶ favor ambulatory treatment whenever possible.

Music. The group morale is significantly improved by suitable music while the patients are waiting for their treatments as well as during the post-treatment period.^{104, 118, 136}

Psychologic Studies

A comprehensive review of the psychologic literature on the shock therapies by Wilcox²²⁶ points out the various theoretic orientations. Some degree of memory loss is frequently found, and the general trend of scores in tests of cognitive function is downward during a course of ECT then returns to or above pre-ECT level within two weeks after the termination of ECT. Most of these studies have been made on patients treated by the standard method.

Intellectual Functioning and Memory. The organic shock syndrome is noted by two German writers. Meyer¹⁴⁰ distinguishes between the organic shock syndrome and the simple shock amnesias with a reversible disturbance in the reproduction of memory material, which he regularly observed in his patients. In general he regards ECT amnesias as of no importance for the therapeutic results and as permitting prognostic deductions only in extreme cases. Schizophrenic thinking disturbances were studied by Gerstacker⁷⁰ in relation to ECT. He used informal interviews with spontaneous productions and also a group of tests to direct thinking processes, such as picture description, sentence construction, re-telling of fables, explanation of proverbs and questions about differences and about contradictions. His patients regularly showed the organic shock syndrome, after which there was likely to be more improvement in their general confusion than in their basic schizophrenic thinking processes, even though the confusion and thinking disturbances usually ran parallel in development. Disconnected thinking proved more responsive to ECT than did flighty thinking.

Brower and Oppenheim³⁷ evaluated fifty cases of various kinds of depression treated three times a week with standard current, and retested one week after the end of the individually determined treatment series with a

large battery of tests. Not only was there no evidence of the organic shock syndrome, but the patients showed an improved capacity to mobilize their intellectual and emotional resources, even without any material alteration in their basic personality structure.

As yet no study has been reported which compares therapeutic results and confusional results on two groups of patients matched for other variables and treated to maximize and to minimize confusion for the two respective groups. This would involve variations in wave form, current intensity, occurrence of convulsion and spacing of treatments. Techniques are now being developed by Wilcox²²⁷ and by Pascal and Zeaman¹⁵⁵ for accurate measurement of confusion.

The impersonal memory material tapped by the Wechsler Memory Scale was found by Dawson⁵⁰ to show a decline a day after ECT but with a return to or above pre-ECT level two weeks later. The contrast between personal and impersonal memory material was studied by Stieper et al.²¹¹ who confirmed the two week post-shock improvement on impersonal material but who found, as Janis and others⁹⁸ had reported earlier, that there tends to be a loss in the field of personal memory. This loss is somewhat greater for recent than for remote memory.

In a search for psychologic test indicators of prognosis with therapy, Scherer¹⁹⁰ studied a group of patients treated with ECT and another group who received lobotomies. Each group had a series of matched controls. Improvement following ECT was significantly related to high pre-test levels of abstraction on Capp's Test of Categorization and low rate of motor speed on the Minnesota rate of manipulation test, also to a low rate of rejections and a high number of movement responses on the multiple-choice Rorschach. This presents a composite picture of the patients who have the better chance for improvement as responsive to their environment, able to think creatively and accurately, but showing motor retardation.

Patients who were receiving a first ECT with Reiter Electrostimulator CW 46 J were studied by Summerskill et al.²¹³ during the post-convulsive period from about one-half hour to two hours after treatment. Orientation for time and speed of tapping were found to be somewhat adversely affected but these investigators did not give weight to the fact that these items were routinely given first in the battery. The Wechsler-Bellevue test, which was presented last in the sequence, showed no significant loss. They concluded that Wechsler-Bellevue type tests are not invalidated by being given shortly after an initial Reiter ECT. A more conservative statement would limit this to at least one hour after treatment and would stress the fact that these observations apply only to a single initial treatment. Similar studies by Wilcox²²⁷ have shown clearly that a time difference of even a

quarter-hour during the post-convulsive period may make gross differences in test responses; also that the post-convulsive confusion after a series of Reiter ECT's may in some cases be greatly different from that after a single isolated treatment.

Kehlet and Lunn¹⁰⁸ studied retrograde amnesia following ECT using meaningful pictures as memory material and also such nonsense material as capital letters and abstract figures. The deficits in recognition lasted less than one-half hour while those for recall were more pronounced.

An analysis of memory below the level of awareness was made by Williams²³¹ who showed that patients treated with BST, and not able after treatment to recall concrete pictures shown before treatment, were, nevertheless, able to recognize ambiguous sketches of these objects with greater accuracy and in shorter time than the control group who had not been shown the concrete picture before.

Personality Changes. During this year psychologists have used a variety of methods to evaluate the personality changes that are observed with ECT. Rojas et al.¹⁷⁶ studied 65 patients before and after ECT with the Szondi test which involves the selection of pictures of patients of various diagnoses. He found consistent selections but no evidence of emotional discharge through ECT action nor of change in the instinct structure. He attributes these results to the lack of change in fundamental psychologic structure, not to the inadequacy of the Szondi as a measuring instrument for this purpose.

The Bender visual-motor gestalt drawing test and human figure drawings have been used qualitatively by Bender and Keeler²⁰ with schizophrenic children undergoing ECT. In addition to the organic signs, which usually disappeared 36 hours after the course of ECT, they found evidence of anxiety and also of distortions different from a regression to a primitive level of drawing. They conclude that with ECT there is a dissolution of the body image but that immediately re-creation is in motion so that new construction and a new integration become possible.

Pascal and Suttell¹⁵⁴ make a quantitative use of the Bender gestalt test, having developed a detailed system of scoring to show amount of pathology. These scores are given for two cases undergoing ECT and are found to parallel closely the general clinical changes.

Using a special series of thematic apperception pictures as a medium, Fisher⁵⁷ studied patients receiving ECT and found 60 per cent to have been stimulated to conscious fears of dying. The patients manifesting clinical improvement showed only moderate conscious and unconscious fear of the treatment while extreme fear was characteristic of those who did not improve. This suggests that the fear is not of therapeutic value.

Repetitive testing of patients throughout a program of therapy which

included ECT of the regressive type advocated by Milligan¹⁴⁵ followed by intensive psychotherapy after the regaining of memory and motor control, is described by Glueck et al.⁷² who used the Wechsler-Bellevue, Rorschach, figure drawing and controlled association tests to measure progress in therapy. Drastic changes took place as seen on all of these measures, but in the particular case cited the improvement took place gradually during the months of psychotherapy. Previous programs of ECT, ICT and psychotherapy alone all had been ineffective. The changes indicated by the tests were in the greater contact with the environment, the better facing of reality, and the creative rather than the autistic use of phantasy.

White and Tanzer²²⁵ report that Rorschachs given to a severely schizophrenic patient one week after the end of ECT and repeated seven weeks later revealed a marked but evanescent personality change, the first record being innocuous and the second that of a very disturbed deteriorated paranoid schizophrenic. They interpret this not as a relapse but as evidence of the extreme masking effects of ECT.

A case study by Bradway³² of a schizophrenic patient before and after ECT and ICT found slight and subtle changes on the Rorschach with variations according to the stage of the illness in a low number of movement, animal movement, and popular responses, the tendency to confabulate and perseverate, the overemphasis on whole responses, the frequency with which the color-form responses outnumbered the form-color responses, and the degree of tendency to responses based on form as the sole determinant.

A group of 20 young male schizophrenics was studied comprehensively by Schwartz¹⁹² with a battery of tests including a Rorschach before and after their ECT therapy. He found that the total personality function of the treated patient remained basically schizophrenic. Superficial and symptomatic changes occurred in the areas of better emotional control and responsibility, more adequate ability to test reality, greater interest in interpersonal relationships and less anxiety and regression. There were no losses in personality functioning. The changes varied considerably in individual patients and could not validly be prognosticated.

A careful study of the prognostic efficacy of the Rorschach in the treatment of schizophrenia by means of ICT, ECT, electronarcosis and leucotomy was made by Rees and Jones.¹⁶⁹ Both Piotrowski's criteria and the Munroe method found significant group differences between the pre-treatment Rorschach responses of schizophrenics who recover and those who fail to improve, but provided no evidence that the Rorschach is of value in selecting individual patients for treatment.

Animal Experimentation. During 1951 the animal experimentation with electroconvulsive stimulation (ECS) has concerned the method of producing

seizures, such as the inhalation of carbon disulfide⁷⁶ and the effects of ECS on learning and on conditioned emotional responses. ECS produced deleterious effects on spatial learning in rats.⁶⁸ As few as four ESC's effectively prevented the latent learning of a water maze.²² The post-ECS retention of a Lashley III water maze habit by specially bred samples of rats found a trend (at the .05 level of confidence) to differences between litters, suggesting the possibility of hereditary differences.²³ No difference in learning ability was found between ECS and E.N. treated young rats when 50 ma. direct current was used for 0.5 seconds, and both groups differed from the controls statistically only, not behaviorally.²⁶

Hunt and Brady⁹¹ have shown that ECS in rats can have the immediate effect of diminishing or virtually eliminating a conditioned emotional response established prior to the convulsive treatment. This is more definite following a series of 21 convulsions (three per day) than a series of 7 (one per day). The conditioned emotional response could, however, be acquired or reacquired following one or two subsequent conditioning trials.³⁴ Five to eight ECS's (one per day) appeared to be the critical minimum number to modify this conditioned emotional response. Retention tests at 30, 60, and 90 days, however, showed that ECS had not entirely destroyed the conditioned emotional response, which reappeared in from 4 to 30 days, but also tended to be extinguished faster by non-reinforcement in the ECS treated rats.³³

Physical Aspects

Electrophysiology. Umlauf et al.²²⁰ made a careful study of the impedance of the human head under the conditions of ECT and showed that the impedance of the head falls as either the voltage or the current applied increases. Thus, with 60 cycle a.c. at 90 volts, the current is approximately 360 ma. and the impedance would be 250 ohms. At 160 volts, the current is about 800 ma. and the impedance 200 ohms. The impedance shift is "instantaneous" so that it occurs during the change of the voltage in the electrical pulses.²⁰⁴ This was explained by Reiter¹⁷¹ on the basis that the skin in contact with the electrodes is a non-uniform surface, thus giving rise to a decrease of resistance with increase in current similar to that found with brush contacts in electric motors and not due to any characteristic of the living tissue. It was readily demonstrated that the impedance changes were the same when the stimulus was applied to a corpse after several hours of refrigeration.²²⁸ Goldring et al.⁷³ have found slow potential changes during ECT, MCT and ICT in patients and in unanesthetized monkeys measured by scalp electrodes and verified in the monkeys by direct transorbital recording from implanted electrodes. These

changes in d.c. potential ranged from 4 to 12 millivolts and took 0.5 to 2 minutes to develop. The polarity changes varied from case to case.

Hilkevitch⁸⁴ using unidirectional "square wave" pulses concluded that the optimal pulse duration is 2 msec. and the optimal interval between pulses is 3 msec. thus giving 200 pulses per sec.

The reader is referred to the chapter on EEG for discussion on EEG changes during and after ECT.

Neurophysiology. The intact brain reacts in a relatively standard tonic-clonic convulsive pattern when adequately stimulated electrically. What mechanism in the brain resists the onset of this chain reaction? What mechanism normally terminates this sequence? What conditions permit prolongation of the clonic phase or a continuous series of convulsions as in status epilepticus? When the adequate convulsive electrical stimulus is given in 0.2 sec. there is an initial jerk accompanying the stimulus and then a pause or latent period and then usually an abrupt onset of the tonic phase. When the electric stimulation is nearer to the convulsive rheobase so that 2 to 20 sec. of stimulation are necessary before the onset of the tonic phase, there is no pause between stimulation and onset of the tonic phase. In fact, almost always if the stimulation is interrupted before the onset of the tonic phase the patient's muscles relax and no convulsion occurs. However, the total sequence of stimulation, latent period, tonic phase, clonic phase and atonic or apnea phase lasts between 45 and 60 sec. in most cases irrespective of how much of that time is used in reaching the convulsive threshold.² Thus the tonic and clonic phases are shortened if the stimulation takes 20 sec. to reach the convulsive level. Furthermore, if the clonic phase is suppressed by continuing the electric stimulation throughout that time period, the internal sequences still proceed at the same rate. Therefore, breathing is resumed at 45 to 60 seconds after the *start* of the *stimulation* irrespective of whether or not the clonic phase has been suppressed. Memory disturbances are less but the therapeutic effect is the same.¹ Ruf¹⁷⁹ was able to prolong convulsions in cats to over an hour by meeting the increased oxygen demand of the brain by giving oxygen and forcing circulation with adrenalin. He deduced that the anoxia of the neurones terminates the convulsion. Holmberg and Lahne⁸⁹ observed that administration of 100 per cent oxygen for one minute before treatment prolonged the convulsion. Possibly the rate of the development of the relative anoxia of the different neurone groups is not affected by suppressing the clonic jerks with continued electrical stimulation. In that case the total duration of the sequence would remain relatively constant whether the cell excitation was maintained by the external stimulation or by its intrinsic processes. Ruf¹⁷⁹ also states that when the clonic phase was prolonged in his experiments, alternating

foci developed in the cortex which maintained the process. Furthermore, if the animal breathed CO_2 and O_2 mixtures, the convulsion was suppressed by the CO_2 . Tönnies²¹⁶ and Jung and Tönnies¹⁰⁰ contend that there is a homeostatic inhibitory mechanism which resists the development of the convulsive state. Alexander^{1, 2} postulates that the central excitatory state becomes inhibitory in the tonic phase and that the clonic phase is the irregular release of that inhibition. Ischlonsky's⁹⁵ principle of induction could also be applied to the inhibitory reactions following stimulation. One aspect of Gualtierotti's studies of centers of inhibition is questioned by Arduini et al.¹¹ They fail to confirm the presence of an inhibitory center for the cerebellum in the region of the mammillary bodies and offer an alternative hypothesis of orthodromic activation of cerebellipetal paths to the cerebellum because the stimuli Gualtierotti used were strong enough to radiate considerably. Liberson et al.¹²⁴ demonstrated that relatively weak stimulation of the uncus produces prolonged apnea, whereas stimulation of the superior, orbital and cingulate gyri is much less effective. Hoff et al.⁸⁸ report that stimulation of the anterior sigmoid gyri of cats produced marked renal ischemia. After repeated stimulations the renal tubule cells showed damage, viz., pyknosis, fragmentation of the nuclei, and severe fatty degeneration. Stern²⁰⁸ reports that two patients, one with thrombosis of the posterior spinal arteries, paraplegia, the other with thrombosis of the left lenticulo-striate artery, right hemiplegia, showed improved function following ECT's possibly by activating undamaged or reserve areas of the CNS.

Biochemistry. Sackler et al.¹⁸³ postulate that adrenal cortical hormones are in certain important essentials counterposed by such "antidynes" as histamine, the sex steroids, insulin and thyroid. ECT, ICT and histamine tend to result at first in an increase and later in a decrease in adrenocortical responses as indicated by the blood eosinophil levels and the lymphocyte-neutrophil ratio.¹⁸³ The complexity of the effects of ECT is illustrated by its tendency to normalize thyroid function. Reiss et al.¹⁷⁰ attempt to explain this by postulating that in cases with initially low thyroid function ECT mobilizes the thyrotropic hormone and in cases with initially high thyroid function ECT inhibits the action of the thyrotropic hormone by mobilizing ACTH. Michael and Brown¹⁴⁴ report a tendency to relative lymphopenia in depressive states which tends to shift to a relative lymphocytosis as the mood improves with successful treatment with ECT. However, each ECT usually induces a transient relative lymphopenia two or three hours after the treatment, indicating an adrenal cortical response. These observations raise the possibility that there is a chronic overactivity of the adrenal cortex in depressive states, which is corrected by temporarily further stimulating it by ECT. Geiser⁶⁹ reports an initial increase in lym-

phocytes and secondary lymphopenia lasting from the second to sometimes as long as the eighth hour after E.N. treatments. Raskin et al.¹⁶⁶ report a similar sequence following ECT's. Hann and Kinzius⁷⁹ measured the blood content of epinephrine by its fluorescence in animals and man following ECT's and found an initial fall during the first 5 minutes post-convulsive, then an overproduction and subsequent decreasing waves of epinephrine level till the initial level was approached 15 minutes post-convulsive. Funkenstein⁶² demonstrates that when the blood pressure was raised by I.V. infusion of epinephrine, mecholyl would reduce it, but not if the blood pressure was raised by I.V. infusions of nor-epinephrine. Patients with basal elevation of blood pressure which decreased following 10 mg. of mecholyl I.M., thus indicating that there was overactivity of an ordinary epinephrine-like substance, tended to respond to ECT, but if the mecholyl produced very little decrease in the blood pressure, indicating an overactivity of nor-epinephrine-like substance, ECT was ineffective.

Steinfeld²⁰⁶ reports that clinical improvement tends to occur if the blood pH drops to 7.1, two minutes after ECT. In those patients whose pH did not drop that much he induced ketosis by diet and then the ECT's did bring the pH down to 7.1 and clinical improvement occurred.

General Physiology. de Bastiani and Pinotti¹⁹ describe in dogs a transient cardiac arrest due to vagus excitation when the electroshock is applied to the head. Lunn¹²⁸ reports a rise of skin temperature immediately following ECT's, apparently due to opening of the arterio-venous anastomoses. McClellan et al.¹³⁷ contrary to some previous reports, claim they found a decided increase in intraocular tension during and for about three minutes after ECT's.

Contraindications and Complications. The most common cause of death associated with ECT is cardiac failure, but there is no satisfactory method for foreseeing which patients may succumb. Plice and Pfister¹⁶⁰ report that many of 50 cases with pre-treatment EKG abnormalities had normal EKG's after ECT. de Cherney⁵³ reported 2 patients with bundle branch block who were treated with ECT without mishap. de la Vigne and Le Pourhiet¹¹⁷ report treating a young man suffering from malignant hypertension with 10 ECT's without mishap, but he died with a cerebral hemorrhage five months later after overeating, suggesting that ECT's may be safer than a heavy meal. Shield et al.¹⁹³ report 89 cases with cardiovascular disease who were treated with ECT. There were four deaths, one of which was attributed to ICT which was given after the course of ECT. Frank⁵⁹ considers that recent coronary occlusion, recent cerebral vascular accident and acute febrile disease are absolute contraindications for ECT. Depressions in old age are often successfully treated with ECT.^{59, 131} ECT should be initiated without delay when indicated even during pregnancy.⁸⁵ Karliner and

Savitsky¹⁰⁷ successfully treated a depressed patient with active pulmonary tuberculosis, using curare controlled ECT, each treatment being preceded by pneumothorax. Osmond¹⁶⁰ gave ECT's to a depressed man with a large tantalum plate in his skull without mishap. On the other hand, death followed the second ECT given to a toxic patient with empyema.⁹

Michael¹⁴³ reports temporary impotence in males following a course of ECT's, normal function being regained within 6 to 10 weeks following the last treatment. Biaggini²⁷ reports decreased spermatogenesis in dogs given electroshock convulsions. Crosa and Viviano⁴⁸ believe that turning the patient on his side, atropine pre-medication, a variety of gags help avoid pulmonary abscess after ECT but do not completely prevent this complication. Gags that keep the jaws too far apart interfere with the swallowing reflex during ECT.^{47, 199}

Neuropathology. Different workers continue to report different results as to what kind, if any, of brain damage is caused by electroshock convulsions either under conditions of therapy or in experimental animals. Scholz and Jötten¹⁹¹ concluded that electroshock convulsions in cats produced reversible spotty anemic areas in the brain, but no permanent damage. Liban et al.¹²³ report a post-ECT death from subarachnoid hemorrhage and wide-spread changes. Allen⁴ reviews the literature and concludes that there is definite possibility that structural damage of the brain may result from ECT. Nielsen¹⁴⁸ reported a death following ECT due to unexplained fever up to 108° F. On the other hand, Meyer and McLardy¹⁴¹ review the literature and report two deaths after ECT. Neither patient showed significant structural changes of the brain.

Indications

The following topical outline follows a psychiatric rating scale under development by Wilcox.²³⁰ Symptoms are subclassified into verbal and non-verbal aspects. A five-point scale is used with "0" as normal and "4+" as maximal degree of abnormal deviation and its continuous presence.

Predominantly Neurotic Symptoms. In general, convulsive therapy is contraindicated in the neuroses except for the depressive components.^{8, 68, 168, 187} Stengel²⁰⁷ reported disappointing results in psychoneuroses with intensive ECT, leaving spotty impairment of memory for many months. They consider intensive ECT contraindicated in hysterics.

(1) Body symptoms. The whole range of psychogenic body symptoms including the more clearcut conversion symptoms in the sensori-motor sphere, the general range of psychosomatic symptoms with and without organ pathology and all the psychogenic aches and pains tend to improve under intensive psychotherapy aided by carbon dioxide therapy and low non-convulsive electrostimulation (low E.S.nc.).^{87, 230}

(2) Anxiety-agitation. Low E.S.nc. often gives relief to both anxiety and agitation, but if the anxiety predominates without significant agitation, CO₂ therapy often is sufficient. On the other hand, if agitation predominates and anxiety is poorly verbalized, convulsive (ECT) therapy is the more effective.²³⁰ Fabing⁵⁵ reports favorable results in acute combat neuroses with low E.S.nc.

(3) Obsessions-compulsions. The experience with CO₂, ECT and ICT has been disappointing in obsessive-compulsive symptom patterns unless they are secondary reactions to depression. In that case, ECT sometimes is effective. However, both low and high E.S.nc. tend to give benefit in this area,²³⁰ although severe obsessive-compulsive symptoms are particularly resistant to treatment and constitute an important indication for psychosurgery.^{103, 185, 188}

(4) Guilt feelings. Neurotic guilt feelings tend to be relieved by CO₂ therapy and low E.S.nc.,^{87, 230} but manic-depressive guilt feelings require ECT.

Overlapping Neurotic and Psychotic Symptoms and Psychopathic Items. These symptoms are grouped together because where the verbal component predominates, CO₂ and E.S.nc. are more indicated, but when the non-verbal component is strongly evident ECT is indicated. Poor judgment, deception and anti-social trends, when not secondary to psychosis respond poorly to all the modalities of physical treatment.

(1) Depression-retardation. Neurotic depression is characteristically more verbal than non-verbal and tends to be benefited by CO₂ therapy and low and high E.S.nc.,^{87, 230} but manic-depressive and involutional depressions which are strongly apparent in facial expression and body reactions respond to ECT and usually fail to be benefited by other treatments.^{8, 51, 68, 106, 135, 168, 187} Campbell⁴¹ urges that ECT be used more promptly in the military service for men suffering from manic-depressive depressions. According to Sargent, those depressions which are worse in the morning associated with early morning wakefulness do well on ECT but those patients who sleep well and the depression gets worse as the day goes along may be made worse by ECT.^{185, 188} Zahle²³⁶ emphasizes the need to give psychotherapy when needed in depressions rather than rely only on ECT. Depressed patients constitute a suicidal risk and prolonged E.S.nc. may be a life saving measure in barbiturate overdosage.^{158, 172-174, 237}

(2) Hate-aggression. When the symptoms are mostly verbal in terms of resentment, bitterness or bottled up hate, CO₂, low and high E.S.nc. are helpful, but if the disturbance is translated into combativeness and homicidal tendencies, ECT is indicated. However, low and high E.S.nc. may be beneficial if carried out in a well-protected environment where extreme abreactions can safely be handled.²³⁰

(3) Poor judgment. The poor judgment of the psychopathic personality is quite resistant to all available treatments. Banay and Krumbiegel¹⁸ used high E.S.nc. intensively in aggressive psychopaths, followed by prolonged psychotherapy. If this poor judgment is secondary to psychotic disturbances of thinking then it will be improved when the psychosis clears.²³⁰

(4) Deception. Conscious deception which persists in spite of ventilative, supportive psychotherapy with good rapport, i.e., psychopathic deception, tends to be difficult to treat with the present physical modalities. If the deception is secondary to psychotic disturbances, then it clears when the psychosis clears up.²³⁰

Predominantly Psychotic Symptoms. The consensus of opinion favors ICT for schizophrenia, reserving ECT for the affective and confusional component.^{51, 106, 135, 162, 168, 185, 187}

(1) Manic-acceleration. Intensive high ECT usually brings manic symptoms under control and relapses can often be prevented by a sufficiently persistent prophylactic program.^{209, 210} Carbon dioxide, low and high E.S.nc. and ICT are usually found to be of no benefit for manic symptoms. However, Alexander³ unexpectedly got results with high E.S.nc. and ICT in a few manics.

(2) Unreality-seclusiveness. Psychotic unreality feelings and seclusive withdrawal tend to improve parallel with the improvement of the psychosis with low and high E.S.nc., low ECT and ICT but the CO₂ effects are very transient. However, neurotic unreality and fugue states often show dramatic symptomatic relief with CO₂.²³⁰

(3) Hallucinations. ICT is the therapy of choice if hallucinations in a relatively clear consciousness are present, but often hallucinations are particularly resistant to all treatments now available. One should not give up therapy without having tried low and high E.S.nc. and ECT.²³⁰

(4) Paranoid reactions. Ideas of reference and various patterns of feelings of persecution do poorly on CO₂ and ECT but in some cases respond to ICT and to low and high E.S.nc.^{87, 230}

(5) Impaired memory. Low E.S.nc. tends to stimulate the memory in all types of memory disturbance. A common complaint with this therapy is that old memories may be uncomfortably vivid.²³⁰

(6) Disorientation. Psychotic disorientation often yields to ECT, ICT and low E.S.nc., but tends not to be affected by CO₂ therapy.²³⁰

(7) Lack of insight. Insight is variously understood but its superficial meaning is "awareness of the presence of mental illness." This type of insight tends to follow improvement with any of the modalities.

Statistics

The lack of uniformity in the analysis of the results of ECT makes generalizations difficult. Gottlieb and Huston⁷⁵ compared brief psychotherapy, ICT and ECT in treating three comparable groups of schizophrenics, respectively, and found no significant difference in the results during a follow-up period of one to four years. Karagulla¹⁰⁵ made detailed statistical comparisons between treated and untreated groups of patients, but concluded only that ECT frequently ameliorates depressive symptoms and renders the illness more bearable. Slater²⁰¹ criticizes Karagulla's statistics; her untreated 1940-1948 group was not treated *because* they had a better prognosis, thus invalidating the comparison with the treated group. Solomon²⁰² reports that nearly 95 per cent of acute committed patients are being paroled home since the systematic but selective application of the various shock therapies and psychosurgery. Bockoven et al.²⁹ report that in 1949, 81 per cent of all committed patients were returned home from the same hospital. Fetterman et al.⁵⁶ report a ten-year follow-up study of 100 patients treated with ECT. No deaths occurred due to treatment but nine of the patients have died in the interim. Approximately 75 per cent of the patients with depressive symptoms were relatively well at the time of review though a third of the improved group had had more than one course of ECT's. Tait and Burns²¹⁴ report a follow-up study of 114 cases of involutional illness, mostly depressions, and consider that ECT with supportive psychotherapy is the method of choice. Palmer et al.¹⁵³ review 455 cases of schizophrenia treated with ECT and only 17.6 per cent were discharged and remained discharged after having had only one course of ECT. They consider that ECT makes schizophrenics better hospital patients and more susceptible to other therapy, including psychotherapy and milieu therapy.

Theory

Therapeutic benefits from ECT are still hard to explain. Sandison¹⁸⁴ postulates that ECT destroys fantasies and restores emotions to a higher level than the "instincts," whereas ICT tends to bring the patient in closer touch with his "instincts." Ploog¹⁶¹ discusses in extensive detail his ideas about psychic counter-regulation resulting from ECT. Benda²¹ attempts to bring the reactions to ECT in line with Selye's general adaptation syndrome, considering the electroshock convulsion as a severe stress to which the body adapts and presumably thereby mobilizes its general defenses better. The details are discussed according to an immediate adrenaline phase and a subsequent hormonal, ACTH phase. Recent speculations that

cerebral mechanisms are analogous to the teleostatic and teleodynamic servomechanisms in the electronic brain open new approaches for the analysis of treatment effects.^{17, 18, 141}

PSYCHODYNAMIC FACILITATION WITH GAS ANESTHETICS

Carbon Dioxide

Clinical Aspects. The carbon dioxide coma treatment of psychoneuroses and psychosomatic conditions has come to popular attention in magazine and newspaper releases. It is generally felt that Meduna has overstressed the harmlessness of the procedure and the lack of need for psychotherapy with it. Baars¹³ supports Meduna's findings but feels that the best results will be obtained if psychotherapy is added. Silver¹⁹⁷ reports on 30 psychoneurotics treated by Meduna's technic with 26 improved but none "cured."

Jackman and Schorr⁹⁶ also substantiate Meduna's claims as to benefits in the neuroses. They present a detailed list of neurotic symptoms which are coded as to frequency and intensity. The patients showed marked improvement after CO₂ treatments as shown by the numerical symptom summary. However, Headlee⁸² failed to observe much gain from CO₂ therapy without psychotherapy.

Milligan¹⁴⁶ reports favorably the use of non-coma CO₂ treatments as an aid to psychotherapy to facilitate abreaction. Sargant and Slater¹⁸⁸ report that CO₂ coma treatments have always failed in obsessives and, if persisted in, the patients usually get worse. Sargant¹⁸⁶ reports the best results with CO₂ therapy in reactive depressives and hysterically predisposed persons.

Potts¹⁶³ reports favorably on the use of CO₂ therapy and followed the Wilcox technic of dream analysis with dramatic gain. He reports improvement in 14 of 16 hysterics, 2 of 4 mixed neurotics, 2 of 3 psychogenic impotents, but in neither of 2 hypochondriacs and only 4 of 10 obsessive-compulsives. There is great need for more standardized diagnostic criteria so that the above results can be compared to other series. Wilcox²⁸⁰ favors an exploratory trial with non-coma CO₂ and "psychopenetration" in neurotics,²²⁹ but if the anxiety begins to build up instead of being released, then it is desirable to switch to non-convulsive electrostimulation under sodium pentothal anesthesia.

MacRae¹³⁰ has made numerous colored moving pictures of patients during CO₂ comas and has classified the reactions under eight headings; viz., six psychomotor patterns: attention, lonesomeness, suffering, rage, fear and unreality; and two autonomic patterns: vagotonia and sympathicotonia. These may appear in relatively pure form or in various combinations. It is of interest that patients rarely spontaneously describe their

feelings as "lonely" or "agony" but often recognize those components when the words are supplied.

The Mental Hygiene Committee of the Michigan State Medical Society⁷ gave an unfavorable report about CO₂ therapy and warns that it may be dangerous if it is administered by unqualified persons. Obviously, that holds true for any treatment. There is no doubt that the treatment can be misused but in practice there has been found a wide margin of safety if the treatment is limited to rather quickly inducing sleep and then immediately allowing the patient to wake up. Any debilitating or febrile disease and hypotension should be considered contraindications.

Physiologic Aspects. Spencer et al.²⁰³ demonstrated a synergic anesthetic effect between thiopental sodium (pentothal sodium) and CO₂. One dog exposed to 40 per cent CO₂ for 45 minutes exhibited damage to its CNS and three months later was sacrificed and found to have toxoplasmosis accompanied by a widely disseminated chronic meningoencephalitis.

Wilcox²³⁰ sometimes uses CO₂ for brief superimposed comas in patients on the verge of awakening from non-convulsive electrostimulation given under sodium pentothal anesthesia. The pentothal changes the reaction to the CO₂ to some extent. A 20 per cent CO₂ to 80 per cent O₂ mixture tends to awaken the patient if he is already quite light, but if the per cent of CO₂ is increased to the point of producing a secondary slowing of respiration, there is a tendency to a snoring pattern which is rare when CO₂ is administered without other medication.

Callaway and McKusick⁴⁰ report that O₂ therapy in cases of emphysema with chronic anoxemia sometimes produces death from accumulation of CO₂ in the system. This paradoxical situation is explained on the theory that the oxygen depresses respiration thus allowing the CO₂ concentration in the alveoli to increase. If the CO₂ tension in the blood has exceeded the respiration stimulation phase, then the added CO₂ produces further depression of the respiration resulting in a death-dealing sequence. Emergency pneumoperitoneum with a positive pressure of from 5 to 7 cm. of H₂O proved to be a life saving measure, apparently by forcing a better exchange of gases in the alveoli.

Hensel⁸³ reports that inhalation of 3 per cent CO₂ brings out shivering in persons who are cold but not when the body is normally warm. Blood plasma histamine rises in anoxia but not if CO₂ is increased, apparently, because the lowered pH activates histaminase.²²² Hall and Hall⁷⁷ report that adding CO₂ to air breathed at high altitudes prolongs useful consciousness but not if the subject has been breathing pure oxygen. The increased cerebral blood flow due to the CO₂ is an aid only if the O₂ supply has been deficient.

Kirstein¹¹² offers evidence that CO₂ tends to stimulate internuncial ac-

tivity. Margaria and Sendroy¹³⁴ report that a 5 per cent CO_2 to 95 per cent O_2 mixture increases the rate of denitrogenation by 20 per cent compared to when 100 per cent O_2 is breathed. This may be helpful in diminishing the incidence of decompression sickness in divers. Carbon dioxide inhibits convulsions possibly by its ease of penetration through to neurone membranes.¹⁴⁷

Schäfer et al.¹³⁹ report that exposure to 3 per cent CO_2 for several days exhausts the adrenaline output. Simonson and Winchell¹³⁸ report that a 5 per cent CO_2 to 95 per cent O_2 mixture decreases the flicker fusion frequency. In other words, it impairs rapid visual discrimination.

The report of Anselmo et al.,¹⁰ *Fatal Poisoning from Carbon Dioxide* regarding exposure to over 10 per cent CO_2 in a contaminated well is misleading. The child was incapacitated by the low oxygen and high carbon dioxide (10.5 per cent O_2 and 12.5 per cent CO_2) and fell into the well with his face in the water for two hours before he could be pulled out. The 80-year-old grandfather became incapacitated and fell into the water with his face above the water but was there for four hours before he was finally brought up. Both were dead but probably died of anoxia rather than due to the CO_2 .

Other Cases

Gilmour⁷¹ describes his use of ether abreaction in anxiety neuroses to help recall traumatic incidents and for the integration of the emotional experience and intellectual understanding. However, if in the first ether analysis the subject begins to recall experiences from before age ten, he says it is better to terminate the interview because those experiences may be too severe to tolerate so quickly. Palmer¹⁵¹ describes three aspects of the ego-organization in relation to ether abreaction therapy, the ego related to the doctor, the inner ego and a sort of watching ego overlooking the other two. Shorvon et al.¹⁵⁴ prefer ether abreaction in the treatment of psychosomatic skin disorders but sometimes they add CO_2 to attain an end point of an ether abreaction.

Lindner¹²⁵ reports his experiences with N_2O for narcoanalytic facilitation. The subjective symptoms are described in detail and the transient accessibility of the untreated schizophrenic is emphasized. The N_2O fails to produce euphoria in endogenous depressions. He considers the procedure useful for differential diagnosis and for evaluation of clinical status of patients after treatment with other therapies.

REFERENCES

- 1 Alexander, L.: Suppression of the clonic phase in electrically induced convulsions in man. *Tr. Am. Neurol. A.* 75:244-247, 1950.

- ² —: Suppression of the clonic phase in electrically induced convulsions in man. *Arch. Neurol. & Psychiat.* 66:236-237, 1951.
- ³ —: Personal communication, 1951.
- ⁴ Allen, I. M.: Cerebral injury with electric shock treatment. *New Zealand M. J.* 50:356-364, 1951.
- ⁵ Anglade, L., Queraud, J., and Fraillon, J.: Électro-narcose et électro-choc prolongé. Technique et premiers résultats. *Ann. méd. psychol.* 109:633-637, 1951.
- ⁶ Anonymous: A fatality from insulin shock therapy. *Treat. Serv. Bull.* 6:183-188, 1951.
- ⁷ Anonymous: Always our very best. *J. Michigan M. Soc.* 50:1057-1058, 1951.
- ⁸ Anonymous: Electroshock therapy. *New York State J. Med.* 51:653-655, 1951.
- ⁹ Anonymous: Death from convulsion therapy. *Brit. M. J.* 2:59, 1951.
- ¹⁰ Anselmo, J. E., Pesigan, D. E., Dizon, G. D., et al.: Fatal poisoning from carbon dioxide: Report of five cases with two deaths. *Philippine M.A.J.* 27:102-105, 1951.
- ¹¹ Arduini, A., Moruzzi, G., and Terzuolo, C.: Elettronarcosi e cervello. *Arch. fisiol.* 50:328-348, 1951.
- ¹² Arikian, N. T.: The necessity of individualization in insulin coma therapy. *Delaware State M. J.* 23:243-244, 1951.
- ¹³ Baars, C. W.: The pharmaco-dynamic treatment of psychoneuroses by use of carbon dioxide inhalation. Preliminary report. *Minnesota Med.* 54:51-53, 1951.
- ¹⁴ von Baeyer, W.: Die Moderne Psychiatrische Schocktherapie. Stuttgart, Thieme, 1951.
- ¹⁵ Banay, R. S. and Krumbiegel, S. E.: The aggressive psychopath. Presented at Am. Psychiat. A. Meet., Cincinnati, Ohio, 1951.
- ¹⁶ Barhash, A. Z.: Psychiatric techniques in medical practice. *J.A.M.A.* 146:1584-1588, 1951.
- ¹⁷ Barrett, E.: Cybernetics as applied to a study of normal and abnormal adjustment mechanisms. *J. Psychol.* 30:11-31, 1950.
- ¹⁸ —: Parkinsonian tremor, manic-depressive psychosis and servomechanisms. *Am. J. M. Sc.* 220:485-489, 1950.
- ¹⁹ de Bastiani, G. and Pinotti, O.: Alterazioni cardiovascolari indotte dall'elettroshock nel cane. *Arch. sc. biol.* 33:488-502, 1949.
- ²⁰ Bender, L. and Keeler, W. R.: The body image of schizophrenic children following electroshock therapy. Presented at Am. Orthopsychiat. A. Meet., Detroit Michigan, 1951.
- ²¹ Benda, P.: Le syndrome général d'adaptation. Ses applications cliniques et thérapeutiques en neuropsychiatrie. *Encéphale.* 40:228-284, 1951.
- ²² Bendig, A. W.: The effects of electroshock convulsions on latent learning in the white rat. *Univ. Pittsburgh Bull.* 48:1-6, 1951.
- ²³ — and Braun, H. W.: The influence of the genotype on the retention of a maze habit in the rat following electroshock convulsions. *J. Comp. & Physiol. Psychol.* 44:112-117, 1951.
- ²⁴ Bergeron, M., and Chertok, L.: Deux cas d'accidents d'insulinothérapie (coma prolongé et état lethargique avec issue favorable). *Ann. méd. psychol.* 109:332-337, 1951.
- ²⁵ Berkwitz, N. J.: Modification of non-convulsive faradic stimulation. Mimeographed instructions, 1951.
- ²⁶ Bernberg, R. E.: A comparison of the effects of electroconvulsive shock and elec-

- tronarcosis upon the learning ability of young rats. *J. Comp. & Physiol. Psychol.* 44:50-60, 1951.
- 27 Biaggini, G. C.: Sulle modificazioni istologiche dei testicoli de cani sottoposti ad elettroshock. *Boll. Soc. ital. biol. sper.* 26:1588-1589, 1950.
 - 28 Billet, J., Pagès, P., Lafon, R., Billet, M., and Billet, B.: Les accidents et incidents de la cure de Sakel. Hypothèses pathogéniques et prévention. *Ann. méd. psychol.* 109:23-40, 1951.
 - 29 Bockoven, J. S., Greenblatt, M., and Solomon, H. C.: Treatment results in the major psychoses. *New England J. Med.* 244:357-361, 1951.
 - 30 Boitelle-Lentulo, C., Boitelle, G., Fallecker, and Hourcard: Hemiplégie transitoire au cours du coma insulinaire. *Abstr. Ann. méd. psychol.* 109:86, 1951.
 - 31 Bonparis, A.: La insulina amorfa en la cura de Sakel. *Rev. Kuba* 6:96, 1950.
 - 32 Bradway, K.: Rorschach records of a schizophrenic patient before, during and after electric shock and insulin treatment. *J. Project. Techniques.* 15:87-97, 1951.
 - 33 Brady, J. V.: The effect of electro-convulsive shock on a conditioned emotional response. The permanence of the effect. *J. Comp. & Physiol. Psychol.* 44:507-511, 1951.
 - 34 — and Hunt, H. F.: A further demonstration of the effect of electro-convulsive shock on a conditioned emotional response. *J. Comp. & Physiol. Psychol.* 44:204-209, 1951.
 - 35 v. Braunmühl, A.: Ein neues Geraet fuer die Heilkrampfbehandlung mittels elektrischen Stromes. *Fortschr. d. Neurol., Psychiat.* 19:325-332, 1951.
 - 36 Brody, M.: Modification of the electroshock convulsion by means of curare, intravenous barbiturate and an airway. *J. Nerv. & Ment. Dis.* 113:211-222, 1951.
 - 37 Brower, D. and Oppenheim, S.: The effects of electroshock therapy on mental functions as revealed by psychological tests. *J. Gen. Psychol.* 45:171-188, 1951.
 - 38 Brussel, J. A. and Schneider, J.: The B.E.S.T. in the treatment and control of chronically disturbed mental patients. A preliminary report. *Psychiatric Quart.* 25:55-64, 1951.
 - 39 Cabitto, L.: L'elettroshockterapia. *Omnia ther.* 2:277-310, 1951.
 - 40 Callaway, J. J. and McKusick, V. A.: Carbon dioxide intoxication in emphysema: Emergency treatment by artificial pneumoperitoneum. *New England J. Med.* 245:9-13, 1951.
 - 41 Campbell, J. D.: Psychiatry and mobilization, *J.A.M.A.* 146:87-93, 1951.
 - 42 Canki, T. T.: Two cases of juvenile schizophrenia. *Delaware State M. J.* 23:240-242, 1951.
 - 43 Cogan, S. and Gross, R. J.: Acute pulmonary changes during insulin coma therapy. *Am. J. Psychiat.* 108:44-45, 1951.
 - 44 Cohen, M.: Analysis of prognostic factors in insulin therapy. *Arch. Neurol. & Psychiat.* 66:412-418, 1951.
 - 45 Constans, J.: Électro-narcose. *Encéphale.* 39:604-636, 1950.
 - 46 Cossa, P. and Martin, P.: Insuline, épilepsie et lobe temporal. *Presse méd.* 58:1326, 1950.
 - 47 Crosa, G.: A proposito di una tecnica di prevenzione della suppurazione polmonare de terapie convulsivanti. *Inform. med., Genova.* 5:1-7, 1951.
 - 48 — and Viviano, M.: La suppurazione polmonare da terapie convulsivanti. *Sistema nerv.* 3:1-8, 1951.
 - 49 Dahl, L.: Some cases of general allergy to insulin in the course of psychiatric treatment with insulin shock. *Acta allergol.* 3:26-38, 1950.

- ⁵⁰ Dawson, J. G.: The effect of electro-convulsive therapy on psychotic patients as measured by the Wechsler memory test. Thesis, University of Chicago, 1947.
- ⁵¹ Dax, E. C.: Indication for shock therapy. *J. Ment. Sc.* 97:142-144, 1951.
- ⁵² De, N.: Histamine and insulin treatment of schizophrenia. *Indian J. Neurol. & Psychiat.* 2:35-46, 1950.
- ⁵³ de Cherney, H. G.: Contraindications for electric shock treatment (The need for re-evaluation). *Delaware State M. J.* 23:226-227, 1951.
- ⁵⁴ Donnelly, J. and Radley-Smith, E. J.: Thrombotic "hydrocephalus" in insulin therapy. *Lancet.* 2:904-909, 1950.
- ⁵⁵ Fabing, H. D.: Non-convulsive electrostimulation therapy (Reiter) in the treatment of combat neuroses in the Korean War. Presented at the Am. Psychiat. A. Meet., Cincinnati, Ohio, 1951.
- ⁵⁶ Fetterman, J. L., Victoroff, V. M., and Horrocks, J. With the assistance of Bregman, E. B.: A ten-year follow-up study of electro-coma therapy. *Am. J. Psychiat.* 108:264-270, 1951.
- ⁵⁷ Fisher, S.: The conscious and unconscious attitudes of patients toward electric shock treatment. *Arch. Neurol. Psychiat.* 65:244, 1951.
- ⁵⁸ Fosmire, F. R. and Brown, W. L.: A preliminary study of the effect of electro-convulsive shock on spatial learning. *J. Genet. Psychol.* 79:69-75, 1951.
- ⁵⁹ Frank, J. A.: Psychiatry and geriatrics: A review. *Am. J. M. Sc.* 222: 109-114, 1951.
- ⁶⁰ Frosch, J., Impastato, D., and Wortis, S. B.: Intensive electroshock treatment with Reiter apparatus. *Am. J. Psychiat.* 108:204-207, 1951.
- ⁶¹ Funderburk, W.: The effect of repeated insulin comas on the EEG. Presented at Central Assoc. of Electroencephalographers Meet., Chicago, Illinois, 1951.
- ⁶² Funkenstein, D.: The role of ordinary epinephrine and nor-epinephrine in the elevation of blood pressure during stress. *J. Nerv. & Ment. Dis.* 113:177-178, 1951.
- ⁶³ —, Greenblatt, M., Solomon, H. C., and Meadow, A.: Nor-epinephrine-like and epinephrine-like substances in psychotic and psychoneurotic patients. Presented at Am. Psychiat. A. Meet., Cincinnati, Ohio, 1951.
- ⁶⁴ —, Greenblatt, M., and Solomon, H. C.: Autonomic changes paralleling psychologic changes in mentally ill patients. *J. Nerv. & Ment. Dis.* 114:1-18, 1951.
- ⁶⁵ Futterman, S.: Recent trends in psychiatry. *Ann. West. Med. & Surg.* 5:3, 1951.
- ⁶⁶ Gans, R. W. and Deutsch, L. P.: Persistent organic and psychogenic syndrome following prolonged insulin coma. *Psychiatric Quart.* 25:424-433, 1951.
- ⁶⁷ Gayle, R. F., Jr.: The role of the general hospital in the care of the mentally ill. *Am. J. Psychiat.* 108:103-106, 1951.
- ⁶⁸ — and Campbell, R. E.: Electroconvulsive therapy. *Dis. Nerv. System* 12:230-235, 1951.
- ⁶⁹ Geiser, M.: Veraenderungen des weissen Blutbildes und des Blutzuckerspiegels als Folge der Elektronarkose. *Monatschr. f. Psychiat. u. Neurol.* 122:47-66, 1951.
- ⁷⁰ Gerstacker, W.: Die schizophrene Denkstörung in der Elektrokrampfbehandlung. *Arch. Psychiat.* 183:423-468, 1950.
- ⁷¹ Gilmour, D.: Ether: an estimation of its use in the treatment of the psychoneuroses. *J. Ment. Sc.* 97:148-158, 1951.
- ⁷² Glueck, B. C., Jr., Krasner, J. D., and Pares, R.: The use of serial testing in regressive electroshock treatment. In Hoch, P. L. and Zubin, J. (eds.): *Relation of Psychological Tests to Psychiatry*. New York, Grune & Stratton, 1951.

- ⁷³ Goldring, S., Ulett, G., O'leary, J., and Greditzer, A.: Initial survey of slow potential changes obtained under resting conditions and incident to convulsive therapy. *Electroencephalog. & Clin. Neurophysiol.* 2:297-308, 1950.
- ⁷⁴ Gordon, G. B. and Weitzner, H. A.: Rheumatoid arthritis and insulin therapy. *J.A.M.A.* 145:842, 1951.
- ⁷⁵ Gottlieb, J. S. and Huston, P. E.: Treatment of schizophrenia. A comparison of three methods: Brief psychotherapy, insulin coma and electric shock. *J. Nerv. & Ment. Dis.* 113:211-222, 1951.
- ⁷⁶ Griffiths, W. J. and Wolfe, J. B.: An easy way to produce convulsions in rats: carbon disulfide. *J. Comp. & Physiol. Psychol.* 43:416-417, 1950.
- ⁷⁷ Hall, F. G. and Hall, K. D.: Effect of adding carbon dioxide to inspired air on consciousness time of man at altitude. *Proc. Soc. Exper. Biol. & Med.* 76:140, 1951.
- ⁷⁸ Halle, L. and Ross, J. F.: Neurological complications of insulin therapy with electroencephalographic studies; case studies. *Arch. Neurol. Psychiat.* 65:703-712, 1951.
- ⁷⁹ Hann, J. and Kinzius, H.: Ueber den Adrenalinspiegel des Blutes beim Elektrokampf. *Deutsche Ztschr. Nerven.* 163:82-92, 1949.
- ⁸⁰ Hasché, E.: Zur Elektroschockbehandlung der Psychosen. *Wien. klin. Wchschr.* 62:725-727, 1950.
- ⁸¹ Hayward, M. L.: The emotional reactions of a schizophrenic patient to shock therapy. *Psychiatric Quart.* 25:288-293, 1951.
- ⁸² Headlee, R.: An analysis of 271 consecutive cases seen by a psychologic service unit in Milwaukee. *Wisconsin M. J.* 50: 161-167, 1951.
- ⁸³ Hensel, H.: Auslösung von Kältezittern durch Kohlensäureatmung. *Arch. ges. Physiol.* 252:107-110, 1949.
- ⁸⁴ Hilkevitch, A.: Frequency and length of stimulus in electric shock therapy. *Arch. Neurol. & Psychiat.* 65:245, 1951.
- ⁸⁵ Hill, A. H. and Keedy, D. M.: Psychoses related to childbirth. *Texas State J. Med.* 47:635-638, 1951.
- ⁸⁶ Himwich, H. E.: *Brain Metabolism and Cerebral Disorders*. Baltimore, Williams & Wilkins, 1951.
- ⁸⁷ Hirschfeld, G. and Bell, J.: Differential cerebral stimulation. *Dis. Nerv. System* 12:264-268, 1951.
- ⁸⁸ Hoff, E. C., Kell, J. F., Jr., Hastings, N., Sholes, D. M., and Gray, E. H.: Vasomotor, cellular and functional changes produced in kidney by brain stimulation. *J. Neurophysiol.* 14:317-332, 1951.
- ⁸⁹ Holmberg, G. and Lahne, B.: Hypoxämien vid elektroshockbehandling. *Nord. med.* 43:1052-1056, 1950.
- ⁹⁰ Holzer, W.: *Therapie der Nerven- und Geisteskrankheiten*. Wien. Maudrich, 1951.
- ⁹¹ Hunt, H. F. and Brady, J. V.: Some effects of electro-convulsive shock on a conditioned emotional response. *J. Comp. & Physiol. Psychol.* 44:88-98, 1951.
- ⁹² Hutter, A.: Die besonderen Formen der Shockbehandlungen, im besonderen die neuen Methoden der Krampfmitigation. *Praxis.* 39:873-877, 1950.
- ⁹³ Impastato, D. J.: Personal communication. 1951.
- ⁹⁴ —, Frosch, J., Robertiello, R. C., and Wortis, S. B.: Improved electroconvulsive therapy with low amperage unidirectional currents. *Dis. Nerv. System.* 12:306-310, 1951.
- ⁹⁵ Ischlondsky, N. E.: *Brain and Behaviour*. St. Louis, Mosby, 1949.

- ⁹⁶ Jackman, A. I. and Shorr, C. A.: Evaluation of CO₂ therapy of the neuroses. Presented at the Am. Psychiat. A. Meet., Cincinnati, Ohio, 1951.
- ⁹⁷ Jannuccelli, C.: L'elettroshock lombo-pubico nel trattamento dell'enuresi in anormali psichici. *Riv. sper. di freniat.* 75:79-94, 1951.
- ⁹⁸ Janis, I. L. and Astrachan, M.: The effect of electroconvulsive treatments on memory efficiency. *J. Abnorm. & Social Psychol.* 46:501-511, 1951.
- ⁹⁹ Jung, R.: Das Elektroenzephalogramm bei der psychiatrischen Shockbehandlung. *Schweiz. Arch. Neurol. u. Psychiat.* 66:421-423, 1950.
- ¹⁰⁰ — and Tönnies, J. F.: Hirnelektrische Untersuchungen ueber Entstehung und Erhaltung von Krampfantladungen: Die Vorgaenge am Reizort und die Bremsfaehigkeit des Gehirns. *Arch. Psychiat.* 185:701-735, 1950.
- ¹⁰¹ Kajtor, F.: Experimentelle Untersuchungen ueber die Hemmungswirkung von Histamin und anderen gefaesserweiternden Mitteln auf die Kraempfe im Cardiazol- und Elektroschock am Menschen. *Arch. Psychiat.* 186:46-58, 1951.
- ¹⁰² —: The anticonvulsive action of histamine and of other vasodilating drugs on experimental convulsions in man. *J. Nerv. & Ment. Dis.* 112:511-525, 1950.
- ¹⁰³ Kalinowsky, L. B.: Principles governing the selection of cases for psychosurgery. *Surg., Gynec. & Obst.* 92:601-603, 1951.
- ¹⁰⁴ Kandler, H. M.: Studying a problem in psychiatric nursing. *Am. J. Nursing.* 51:108-111, 1951.
- ¹⁰⁵ Karagulla, S.: Evaluation of electric convulsion therapy as compared with conservative methods of treatment in depressive states. *J. Ment. Sc.* 96:1060-1091, 1950.
- ¹⁰⁶ Karlner, W.: Shock treatments in psychiatry. *Am. Practitioner.* 2:511, 1951.
- ¹⁰⁷ — and Savitsky, N.: Electroshock therapy in the presence of pulmonary tuberculosis. *Dis. Nerv. System.* 12:186-189, 1951.
- ¹⁰⁸ Kehlet, H. and Lunn, V.: Den retrogade amnesi efter electroshockbehandling. *Nord. med.* 45:716-719, 1951.
- ¹⁰⁹ Kerman, E. F.: Dramamine in the prevention and treatment of nausea and vomiting following electroshock therapy. *Dis. Nerv. System.* 12:83-85, 1951.
- ¹¹⁰ Kersley, G. D., Mandel, L., Jeffrey, M. R., Bene, E., and Taylor, K. B.: Hypoglycemia in treatment of rheumatoid arthritis. *Brit. M. J.* 2:574-578, 1951.
- ¹¹¹ —, Mandel, L., Taylor, K. B., and Jeffrey, M. R.: Spontaneous hypoglycemia after insulin therapy in rheumatoid arthritis. *Brit. M. J.* 2:578-580, 1951.
- ¹¹² Kirstein, L.: Early effects of oxygen lack and carbon dioxide excess on spinal reflexes. *Acta physiol. scandinav. Suppl.* 23:80, 1-54, 1951.
- ¹¹³ Koenig, J. H. and Feldman, H.: Nonstandard method of electric shock therapy. *Psychiatric Quart.* 25:65-72, 1951.
- ¹¹⁴ Korson, S. M.: Spinal anaesthesia with electroshock therapy in a case complicated by recent fracture. *Dis. Nerv. System.* 12:337-339, 1951.
- ¹¹⁵ Kraemer, R.: Beobachtung bei der Behandlung mit subkonvulsiven Cardiazolstoessen. *Deutsche med. Wchnschr.* 75:1081-1083, 1950.
- ¹¹⁶ Larragoiti, R. J.: Estimulacion diencephalica. *Arch. Neurol. y Psychiat.* 6:1-4, 1951.
- ¹¹⁷ de la Vigne, A. R. and Le Pourhiet: Mélancolie chez un hypertendu avec séquelles d'un ictus. Guérison par électro-choc. *Ann. méd. psychol.* 109:66-69, 1951.
- ¹¹⁸ Leedy, J. J. and Leedy, D. J.: Use of music with electroconvulsive therapy. *Dis. Nerv. System.* 12:281-283, 1951.
- ¹¹⁹ Levy, S.: Narcosynthesis immediately following insulin shock: A five year follow-up. Presented at Am. Psychiat. A. Meet., Cincinnati, Ohio, 1951.

- ¹²⁰ Levy, S.: Progress in psychiatry in 1950. *Clin. Med.* 58:179-189, 1951.
- ¹²¹ — and Southcombe, R. H.: Value of convulsive therapy in juvenile schizophrenia. *Arch. Neurol. & Psychiat.* 65:54-59, 1951.
- ¹²² Lewis, N. D. C.: A report on the research program of the psychiatric institute, 1950. *Psychiatric Quart. Suppl.* 25:1-22, 1951.
- ¹²³ Liban, E., Halpern, L., and Rozanski, J.: Vascular changes in the brain in a fatality following electroshock. *J. Neuropath. & Exper. Neurol.* 10:309-318, 1951.
- ¹²⁴ Liberson, W. T., Scoville, W. B., and Dunsmore, R. H.: Stimulation studies of the prefrontal lobe and uncus in man. *Electroencephalog. & Clin. Neurophysiol.* 3:1-8, 1951.
- ¹²⁵ Lindner, M.: Ueber die Verwendung der Lachgas-Beatmung in der Psychiatrie. *Arch. Psychiat.* 186:586-602, 1951.
- ¹²⁶ Lipton, M. B., Tamarin, S., and Lotesta, P.: Test evidence of personality change and prognosis by means of the Rorschach and Wechsler-Bellevue tests on 17 insulin treated paranoid schizophrenics. *Psychiatric Quart.* 25:434-444, 1951.
- ¹²⁷ Lorentzen, K. A.: The central nervous system during insulin shock, with special reference to structural activity changes of the nerve cells. An experimental histological study. *Acta psychiat. et. neurol. Suppl.* 64:1-83, 1950.
- ¹²⁸ Lunn, V.: Experimental studies on electroshock treatment. II. Variations in the skin temperature following E. C. T. *Acta psychiat. et. neurol.* 26:7-48, 1951.
- ¹²⁹ Mace, N. C., Pollock, F. R., and Feld, M.: Insulin shock therapy. *Dis. Nerv. System.* 12:178-180, 1951.
- ¹³⁰ MacRae, L. D.: Reaction patterns seen during carbon dioxide comas. Unpublished manuscript, 1951.
- ¹³¹ Madden, J. J., Luhan, J. A., Kaplan, L. A., and Reidy, J. J.: Psychoses of later life. *Illinois M. J.* 100:127-132, 1951.
- ¹³² Magruder, L. F.: Development of electric shock therapy at East Louisiana State Hospital. *New Orleans M. & S. J.* 104:25-27, 1951.
- ¹³³ Malamud, W.: Schizophrenia and hormones: Some present trends: their implications and backgrounds. *New England J. Med.* 244:908-914, 1951.
- ¹³⁴ Margaria, R. and Sendroy, J.: Effect of carbon dioxide on rate of denitrogenation in human subjects. *J. Appl. Physiol.* 3:295-308, 1950.
- ¹³⁵ Mayer-Gross, W.: Insulin coma therapy of schizophrenia: Some critical remarks on Dr. Sakel's report. *J. Ment. Sc.* 97:132-135, 1951.
- ¹³⁶ McCartney, J. L.: Five years of private psychiatry *Quart. Rev. Psychiat. & Neurol.* 6:249-251, 1951.
- ¹³⁷ McClellan, J. W., Mills, M., Jr., and Markson, J. W.: Measurement of intra-ocular tension in insulin and electroconvulsive therapy. *Bull. Menninger Clin.* 14:220-225, 1950.
- ¹³⁸ Metman, P.: Notes on the post-insulin analysis of a schizophrenic man. *Brit. J. M. Psychol.* 24:55-63, 1951.
- ¹³⁹ Mewhort, E.: An insulin therapy cart. *Am. J. Nursing.* 50:737-738, 1950.
- ¹⁴⁰ Meyer, J. E.: Ueber Schockamnesien und ihre Beziehung zum Heilverlauf der Psychosen. *Arch. Psychiat.* 186:254-263, 1951.
- ¹⁴¹ Meyer, A. and McLardy, T.: Neuropathology in relation to mental disease. *Recent Progr. Psychiat.* 2:284-323, 1950.
- ¹⁴² Meyers, D. and Shurley, J. T.: A study of the etiology and management of the

- phenomenon of insufficient response to the usual termination of hypoglycemic stupor occurring in insulin therapy of psychoses. Unpublished manuscript, 1951.
- ¹⁴³ Michael, S. T.: Impotence during electric shock therapy. *Psychiatric Quart.* 25:24-31, 1951.
 - ¹⁴⁴ — and Brown, W. T.: Blood lymphocytes and adrenal function in electric convulsive therapy. *J. Nerv. & Ment. Dis.* 118:538-548, 1951.
 - ¹⁴⁵ Milligan, W. L.: Non-convulsive stimulation therapy. A new psychiatric treatment. *Lancet.* 1:938-939, 1951.
 - ¹⁴⁶ —: Treatment of psychoneurosis. Modified CO₂ abreactive technique. *Brit. M. J.* 1:1426-1428, 1951.
 - ¹⁴⁷ Moussatché, H.: Ação inibidora do gás carbonico sobre as convulsões experimentais III. Experiencias na crioepilepsia da rã. Mecanismo da ação inibidora do gás carbonico nas convulsões. *Mem. Inst. Oswaldo Cruz.* 48:219-226, 1950.
 - ¹⁴⁸ Nielsen, J. M.: Death following electroshock treatment; report of a case. *Bull. Los Angeles Neurol. Soc.* 15:200-201, 1950.
 - ¹⁴⁹ O'Flanagan, P. M., Timothy, J. I., and Gibson, H. G.: Further observations on the use of combined photic and chemically induced cortical dysrhythmia in psychiatry. *J. Ment. Sc.* 97:174-190, 1951.
 - ¹⁵⁰ Osmond, H.: An account of E. C. T. given to a patient with a tantalum plate in his skull. *J. Ment. Sc.* 97:381-387, 1951.
 - ¹⁵¹ Palmer, H.: Three aspects of ego-organization in relation to ether abreaction therapy. *J. Ment. Sc.* 97:388-393, 1951.
 - ¹⁵² Palmer, D. M. and Garrett, E. S., Jr.: Schizophrenia treated with insulin shock followed by electroshock therapy. *Ohio State M. J.* 47:435-437, 1951.
 - ¹⁵³ —, Sprang, H. E., and Hans, C. L.: Electroshock therapy in schizophrenia. A statistical survey of 455 cases. *J. Nerv. & Ment. Dis.* 114:162-171, 1951.
 - ¹⁵⁴ Pascal, G. R. and Suttell, B. J.: The Bender-Gestalt Test, Quantification and Validity for Adults. New York, Grune & Stratton, 1951.
 - ¹⁵⁵ — and Zeaman, J. B.: Measurement of some effects of electroconvulsive therapy on the individual patient. *J. Abnorm. & Social Psychol.* 46:104-114, 1951.
 - ¹⁵⁶ Pearson, J. S. and Swenson, W. M.: A note on extended findings with the M M P I in predicting response to electro-convulsive therapy. *J. Clin. Psychol.* 7:288, 1951.
 - ¹⁵⁷ Pflugfelder, G.: Psychologische Untersuchungen ueber Bewusstseinstoerungen in der Insulinkur. Monograph, *Monatschr. f. Psychiat. u. Neurol.* Basel- New York, Karger, 1951.
 - ¹⁵⁸ Pinch, C. and Geoghegan, J. J.: Barbiturate poisoning treated with modified electrotherapy. *Canad. M.A.J.* 64:233-234, 1951.
 - ¹⁵⁹ Plattner, P. and Löhnis, H.: Ueber krampffreie Elektrobehandlung depressiver Zustände. *Monatschr. f. Psychiat. u. Neurol.* 108:209-222, 1943.
 - ¹⁶⁰ Plice, S. G. and Pfister, C. W.: Electrocardiographic abnormalities in the mentally ill; is "myocardial damage" sometimes of psychogenic origin? *Illinois M. J.* 99:212-217, 1951.
 - ¹⁶¹ Ploog, D.: "Psychische Gegenregulation" dargestellt am Verlauf von Elektroshockbehandlungen. *Arch. Psychiat.* 183:617-663, 1950.
 - ¹⁶² Polatin, P.: Schizophrenia. In *Current Therapy* 1951. Philadelphia, Saunders, 1951.
 - ¹⁶³ Potts, F.: Tratamiento farmacologico de las neurosis con el dioxido de carbono. *Arch. Neurol. y Psiquiat.* 6:5-10, 1951.
 - ¹⁶⁴ Quarti, C.: Contribution a l'étude de l'électronarcose (Thérapeutique psychia-

- trique. Méthode d'investigation clinique expérimentale.) Presse méd. 59:125-127, 1951.
- ¹⁶⁵ Rackow, L. L.: Modified insulin, psychodrama, and rehabilitation techniques in the treatment of anxiety and tension states. Unpublished manuscript, 1951.
 - ¹⁶⁶ Raskin, N., Howard, G., and Singer, S.: Lymphocytic and eosinophilic reaction to electric shock treatment. *Am. J. Psychiat.* 107:758-763, 1951.
 - ¹⁶⁷ Rees, L.: Insulin therapy. *Recent Progr. Psychiat.* 2:635-660, 1950.
 - ¹⁶⁸ Rees, T. P.: A note on the indications for shock therapy. *J. Ment. Sc.* 97:144-145, 1951.
 - ¹⁶⁹ Rees, W. L. and Jones, A. M.: An evaluation of the Rorschach test as a prognostic aid in the treatment of schizophrenia by I. C. T., electronarcosis, E. C. T. and leucotomy. *J. Ment. Sc.* 97:681-689, 1951.
 - ¹⁷⁰ Reiss, M., Hemphill, R. E., Maggs, R., Haigh, C. P., and Reiss, J. M.: Comparative action of E. C. T. and of pituitary anterior lobe hormones on thyroid function. *Brit. M. J.* 2:634-637, 1951.
 - ¹⁷¹ Reiter, R.: Personal communication, 1940.
 - ¹⁷² Robie, T. R.: Electrostimulatory therapy as immediate antidote for barbiturate poisoning. *J. Nerv. & Ment. Dis.* 113:352-359, 1951.
 - ¹⁷³ —: Electrostimulatory therapy as immediate antidote for barbiturate poisoning. *Arch. Neurol. & Psychiat.* 66:221-223, 1951.
 - ¹⁷⁴ —: Treatment of acute barbiturate poisoning by nonconvulsive electrostimulation. *Postgraduate Med.* 9:253-255, 1951.
 - ¹⁷⁵ Robinson, D. H.: The insulin unit at the New Jersey State Hospital, Trenton. Presented at Am. Psychiat. A. Meet., Cincinnati, Ohio, 1951.
 - ¹⁷⁶ Rojas, N., Belbey, J., and Szekely, B.: El Szonditest y las modificaciones psíquicas producidas por el electroshock. *Día méd.* 23:216, 1951.
 - ¹⁷⁷ Rothschild, D., Van Gordon, D. J., and Varjabedian, A.: Regressive shock therapy in schizophrenia. *Dis. Nerv. System.* 12:147-150, 1951.
 - ¹⁷⁸ Rowe, C. J., Schiele, B. C., and Labree, G. W.: Electroconvulsive therapy in psychoses complicated by cardiovascular disease. *Journal Lancet.* 71:323-326, 1951.
 - ¹⁷⁹ Ruf, H.: Experimentelle, ueber Stunden dauernde Verlaengerung des Elektrokampfes durch Sauerstoff und Kreislaufmittel. *Nervenarzt.* 21:109-113, 1950.
 - ¹⁸⁰ Russek, H. I., Zohman, B. L., and Tamarin, S. L.: Prophylactic value of papaverine in insulin shock therapy. *New York State J. Med.* 50:2299-2301, 1950.
 - ¹⁸¹ Sackler, M. D., Sackler, R. R., Sackler, A. M., LaBurt, H. A., Van Ophuijsen, H. W., and Co Tui.: Some physiologic common denominators of histamine, sex steroids, insulin and electric convulsive therapies. *Psychiatric Quart.* 25:213-236, 1951.
 - ¹⁸² —, Sackler, R. R., Sackler, A. M., and Van Ophuijsen, J. H. W.: The technique of histamine biochemotherapy and suggestions for its use in psychiatry. *J. Nerv. & Ment. Dis.* 113:40-51, 1951.
 - ¹⁸³ Sackler, R. R., Sackler, M. D., Van Ophuijsen, J. H. W., Co Tui, and Sackler, A. M.: An appraisal of the current status of histamine biochemotherapy in psychiatry and the theoretical significance of its effects. *J. Clin. & Exper. Psychopath.* 12:5-14, 1951.
 - ¹⁸⁴ Sandison, R. A.: The psychology of electric convulsion treatment. *J. Ment. Sc.* 96:734-744, 1950.
 - ¹⁸⁵ Sargant, W.: Discussion on indications for shock therapy. *J. Ment. Sc.* 97:135-139, 1951.

- 186 —: The mechanism of "conversion." *Brit. M. J.* 2:311-316, 1951.
- 187 — and Slater, E.: Physical methods of treatment in psychiatry. *Brit. M. J.* 1:1315-1319, 1951.
- 188 — and Slater, E.: The treatment of obsessional neuroses. *Proc. Roy. Soc. Med.* 43:1007-1010, 1950.
- 189 Schäfer, K. E., Klein, H., and Zinck, K. H.: Experimentelle Untersuchungen ueber den Zusammenhang von Mark und Rinde der Nebennieren unter langdauernder CO₂ Einwirkung. *Klin. Wchnschr.* 28:179-184, 1950.
- 190 Scherer, I. W.: Prognoses and psychological scores in electroconvulsive therapy, psychosurgery and spontaneous remission. *Am. J. Psychiat.* 107:926-931, 1951.
- 191 Scholz, W. and Jötten, J.: Durchblutungsstörungen im Katzenhirn nach kurzen Serien von Elektrokrämpfen. *Arch. Psychiat.* 186:264-279, 1951.
- 192 Schwartz, S. S.: The determination and evaluation of changes in the personality functioning of electroconvulsive treated schizophrenics. Thesis, New York University, 1950.
- 193 Shield, J. A., McCue, H. M., Jr., and Tucker, W. M.: Experiences with electroshock treatment in known cardiovascular disease. *South. M. J.* 43:409-412, 1950.
- 194 Shorvon, H. J., Rook, A. J., and Wilkinson, D. S.: Psychological treatment in skin disorders, with special reference to abreactive techniques. *Brit. M. J.* 2:1300-1304, 1950.
- 195 Shurley, J. T.: Current practices in deep insulin therapy of the psychoses. (Round Table). *Am. Psychiat. A. Meet., Cincinnati, Ohio*, 1951.
- 196 Silfverskiöld, W.: Prophylactic neostigmine in electroconvulsive treatment. *Lancet.* 1:1054, 1950.
- 197 Silver, G. A.: Carbon dioxide therapy. *North Carolina M. J.*, 12:486-488, 1951.
- 198 Simonson, E. and Winchell, P.: Effect of high carbon dioxide and low oxygen concentration on fusion frequency of flicker. *J. Appl. Physiol.* 3:637-641, 1951.
- 199 Singer, L.: Électrochocs et abcès du poumon. *Cahiers Psychiat.* 116-127, 1949.
- 200 Singh, K.: Intensive electric convulsive therapy in a military hospital. *Indian M. Gaz.* 85:41-43, 1950.
- 201 Slater, E. T. O.: Evaluation of electric convulsion therapy as compared with conservative methods of treatment in depressive states. *J. Ment. Sc.* 97:567-569, 1951.
- 202 Solomon, H. C.: Treatment of the psychoses. *Psychiatric Quart.* 25:1-19, 1951.
- 203 Spencer, J. N., Parry, T. M., Whithead, R. W., and Draper, W. B.: Tolerance of dog under thiopental sodium anesthesia to high concentrations of carbon dioxide. *J. Pharmacol. & Exper. Therap.* 98:366-372, 1950.
- 204 Spiegel, E. A., Spiegel-Adolf, M., and Lee, A. S. J.: Physiological and physiochemical mechanisms in electric shock treatment. Unpublished manuscript, 1950.
- 205 Steinfeld, J. I.: Modified methods of electroshock therapy. *In Therapeutic Studies on Psychotics*, Des Plaines, Illinois, Forest Press, 1951.
- 206 Steinfeld, J. I.: Acidosis and its therapeutic value in the treatment of psychotics. *J.A.M.A.* 145:226-227, 1951.
- 207 Stengel, E.: Intensive E.C.T. *J. Ment. Sc.* 97:139-142, 1951.
- 208 Stern, M. M.: Observations on the effect of electroshock in two neurological cases. Unpublished manuscript, 1951.
- 209 Stevenson, G. H.: The prevention of recurring manic-depressive illnesses. *Canad. M.A.J.* 64:198-200, 1951.

- 210 — and Geoghegan, J. J.: Prophylactic electroshock—A five year study. *Am. J. Psychiat.* 10:743-748, 1951.
- 211 Stieper, D. R., Williams, M., and Duncan, C. P.: Changes in impersonal and personal memory following electro-convulsive therapy. *J. Clin. Psychol.* 7:361-366, 1951.
- 212 Stockings, G. T.: *Metabolic Brain Diseases and Their Treatment*. Baltimore, Williams & Wilkins, 1947.
- 213 Summerskill, J., Seeman, W., and Meals, D. W.: An evaluation of post-electroshock confusion with the Reiter EST apparatus. Presented at Am. Psychol. A. Meet., Chicago, Illinois, 1951.
- 214 Tait, C. D. Jr. and Burns, G. C.: Involutional illnesses. A survey of 379 patients, including follow-up study of 114. *Am. J. Psychiat.* 108:27-36, 1951.
- 215 Thompson, O. S. and Norton, A.: Use of gallamine triethiodide (flaxedil) in modifying E. C. T.; a comparison with d-tubocurarine chloride and decamethonium iodide. *Brit. M. J.* 1:857-860, 1951.
- 216 Tönnies, J. F.: Die Erregungssteuerung im Zentralnervensystem. Erregungsfokus der Synapse und Rueckmeldung als Funktionsprinzipien. *Arch. Psychiat.* 182:478-535, 1949.
- 217 Treves, G. and Coda, G.: Tecnica, azione, indicazioni della narco-shock-terapia. *Rass. stud. psichiat.* 39:750-759, 1950.
- 218 Tsai, S. Y., Bennett, A., May, L. G., and Gregory, R. L.: Effect of insulin hypoglycemia on eosinophiles and lymphocytes of psychotics. *Proc. Soc. Exper. Biol. & Med.* 74:782-784, 1950.
- 219 Tyler, D. B.: The mechanism of the production of brain damage during insulin shock. *Am. J. Physiol.* 131:554-560, 1941.
- 220 Umlauf, C. W., Gunter, R. C., Jr., and Tunnicliffe, W.: Impedance of the human head as observed during electro-shock treatment. *Confinia neurol.* 11:129-138, 1951.
- 221 Van Amberg, R. J.: The use of insulin sub-coma therapy in the treatment of anxiety states. Presented at Am. Psychiat. A. Meet., Cincinnati, Ohio, 1951.
- 222 Vidal Sivilla, S., Larralde, J., and Jimenez-Vargas, J.: Efectos de la anoxia e hipercapnia sobre la concentracion de histamina del plasma sanguineo. *Rev. españ. fisiol.* 4:327-332, 1949.
- 223 Vogt, M.: The role of hypoglycaemia and adrenaline in the response of the adrenal cortex to insulin. *J. Physiol.* 114:222-233, 1951.
- 224 Weinland, W. L. and Weinland, G.: Ueber elektroencephalographische Beobachtungen beim Insulinschock. *Arch. Psychiat.* 183:34-44, 1949.
- 225 White, A. M. and Tanzer, M.: Rorschach differences and electroshock: A case report. *Psychol. Serv. Cent. J.* 2:46-54, 1950.
- 226 Wilcox, K. W.: Psychological studies in electroshock therapy. *Papers Michigan Acad. Sc., Arts & Let.* 35:357-368, 1951.
- 227 —: The measurement of confusion in shock treated patients. Unpublished manuscript, 1951.
- 228 Wilcox, P. H.: Unpublished data, 1940.
- 229 — and Adler, I.: Shock therapy. In Spiegel, E. A. (ed.). *Progress in Neurology and Psychiatry*, New York, Grune & Stratton, 1951.
- 230 —: Unpublished data, 1951.
- 231 Williams, M.: Memory studies in electric convulsive therapy. II. The persistence of verbal response patterns. *J. Neurol., Neurosurg. & Psychiat.* 13:314-319, 1950.

- ²³² Wilson, L.: Recent advances in apparatus used for electroconvulsant therapy and electronarcosis. *M. J. Australia*. 1:451-453, 1949.
- ²³³ Wortis, J.: Review of psychiatric progress in 1950. Physiological treatment. *Am. J. Psychiat.* 107:519-523, 1951.
- ²³⁴ —: Treatment. In *Soviet Psychiatry*, Baltimore, Williams & Wilkins, 1950 Chap. VIII.
- ²³⁵ Yagdjoglou, B.: Un nouveau procédé technique dans le choc à l'insuline. *Presse méd.* 58:1287-1288, 1950.
- ²³⁶ Zahle, V.: On manic-depressive psychosis and neurosis. *Acta psychiat. et neurol.* 26:95-111, 1951.
- ²³⁷ Zimmerman, G. Jr.: Electrostimulation in respiratory emergency. *J.A.M.A.* 146:1025-1026, 1951.

Psychiatric Nursing and Occupational Therapy

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PSYCHIATRIC NURSING

ARTICLES about organization of psychiatric nurses within the nursing profession and about demarcation of their role and functions have predominated the past year.

Personnel. A temporary committee is investigating what can be done to unify psychiatric nurses without separation from the main body of professional nurses. As a first step, Illinois organized a psychiatric section under the state nurses' association and sent a paid delegate to represent it at the 1951 meeting of the American Psychiatric Association. "The Inventory and Qualifications of Psychiatric Nurses," referred to last year, has greatly helped to give nurses a sense of unity. The data show 9100 psychiatric nurses to be in 600 institutions (some did not participate), nearly half of whom are in public psychiatric hospitals. About 1500 (18 per cent) are head nurses or assistant head nurses, while less than 6 per cent teach in nursing schools. Almost half are aged 20 to 30 years, and only 12 per cent are past 50. The 650 men comprise 7 per cent of the total. Of the 1800 (20 per cent) who have special education beyond that of basic training, half took their work in college or university. About half of the entire group would like part-time graduate study, and 10 per cent further full-time study. These data are helpful to organizations studying general problems of psychiatric nursing.

Education. Leaders of nursing organizations estimate a shortage of 65,000 nurses, one cause of this being attributable to the fact that only 10 per cent of all nursing schools belong to the general education system. Only 1.2 per cent of college and university enrollees are nursing students, whereas 78 per cent of students in the 1190 schools of all types come directly from high school.¹⁷ This fact widens the gap between qualifications for professional nurse training and the trend for college degrees in psychiatric nursing.

The National Institute of Mental Health has continued its grants to expand teaching programs in medical schools, universities and other train-

ing centers; these grants include stipends to graduate students in psychiatric nursing.

A conference held at the University of Cincinnati discussed methods to improve advanced educational courses and incorporate new developments in psychiatric and mental health nursing. The conference recommended a second meeting in 1952 and asked the National League of Nursing Education to initiate plans and help obtain funds.²⁹

Investigating the preparation of students for psychiatric affiliation, Smith³² sent queries to 115 psychiatric nurse instructors in 93 schools in 35 states. Smith concluded that for proper orientation of both faculty and students a long range program is necessary. Advance field trips help students in small groups. General hospitals, even those without psychiatric units, provide a chance to acquaint students with cases of drug toxicity, postoperative disorientation, senile confusion and certain organic psychoses, as preparation for affiliate work. Matheney's study²⁵ showed that 85 students in 8 hospital schools of the New York City area failed in over half their attempts to identify dynamic factors in mental patients' behavior. Matheney recommends more classroom discussion, with clear differentiation between mental symptoms and motivation. Jeffers²² suggests wide use of community resources to give nursing students full information on all aspects of marriage and family life, as a better preparation for both professional and private life.

Two new textbooks are useful in psychiatric affiliation courses: Cunningham's *Psychology for Nurses*¹¹ is helpful for beginners, while Cooley's *Social Aspects of Illness*¹⁰ emphasizes the social problems met by the psychiatric nurse and social worker.

Several articles concern the selection and training of psychiatric aides and technicians. At Little Rock State Hospital two workers⁵ found the Minnesota Multiphasic Personality Inventory effective in detecting psychopathy but ineffective in detecting hypochondriasis, hysteria or hypomania in candidates. These writers recommend the aide with a 10th grade education as the best risk. Using the Revised Beta Examination and the Multiple Choice Rorschach, Yerbury et al.³⁷ selected 95 per cent of very good and 32 per cent of very poor aides, but failed to detect marginal groups. They advise research on a larger battery of tests in the selection and placement of aides. New Jersey¹⁸ continues to emphasize its intensive one-year course for psychiatric technicians. All these efforts are laudable, since only a few of the 80,000 aides working in mental hospitals have had appreciable training. However, a round table discussion of this topic at the 1951 meeting of the American Psychiatric Association pointed out that technicians tend to demand similar pay and occupational status, although their training at best is inferior to that of psychiatric nurses.

Reports continue regarding effective use of volunteer workers in psychiatric wards. A Missouri state hospital recruits and trains various college students for two hours' work each Saturday during the school year.²¹ Boston Psychopathic Hospital volunteer workers spent some 73,000 hours in 1950 on the 117-bed wards.³³ The VA hospitals report increasing use of volunteers.¹⁶ In the 34 VA hospitals with mostly mental patients, about 20,000 regularly scheduled volunteers work 80,000 hours a month. Additional volunteers work with the psychiatric patients in 100 other VA hospitals. Hospital staffs orient, instruct and supervise these volunteers, whose number has grown yearly since inauguration of the plan in 1945. Besides their valuable nursing help, these workers help educate the community in the problems of mental illness. Davis's handbook¹² is useful for volunteers working in mental hospitals.

Therapy. In care of psychologic casualties in case of atomic disaster, Stevens³⁴ emphasizes that people need to see their leaders and to join teams in helping victims. Instruction in use of Geiger counters to measure exposure to radiation prevents fear. Nurses must be able to recognize beginning hysteria and to put every able person to work at a definite task.

Aushman² describes the nurse's part in care of cerebral palsy, while Greiling²⁰ discusses that of myasthenia gravis. Bellam⁶ outlines the careful emotional preparation and care of a child before and after tonsillectomy. Bakwin's⁴ excellent article summarizes for the nurse new research material including evidence that the mother's emotional states do influence fetal activity and heart rate and that lack of oxygen during birth often results in the child's later behavioral changes and neurologic disturbances. It is emphasized that behavior disorders associated with anoxic cerebral damage have a good outlook in cases of early diagnosis and proper treatment. Other important aspects of child care are discussed.

Nace²⁸ has a good article on the care of the aged in a state mental hospital. Zeman³⁸ describes affiliated study by graduate nurses in an institution for elderly people. Newton's book on geriatric nursing³⁰ is the first comprehensive textbook in the field, and is a most practical approach to the subject.

Of special interest is the growing discussion about the role of the psychiatric nurse. The paper by Bennett and Eaton referred to last year has now appeared.⁷ It defines ways in which the psychiatrist can more fully use a competent nurse's abilities, including the disputed function of psychotherapy. Dix¹⁴ insists that the nurse must understand the essential nature of psychotherapy in order to apply its principles to daily nursing. Results of a group psychotherapy project conducted since 1949 by nurses and attendants in a Massachusetts state hospital have been most satisfactory, according to Kaldeck,²³ who describes ways of selecting and training group leaders. Kremsdorf's²⁴ excellent article shows how the nurse's increasing

participation as therapist, her supervision of other personnel and her organization of all pertinent data about the patient make her the psychiatrist's invaluable assistant in handling a larger number of patients. Mereness²⁶ also emphasizes the nurse's important function as part of the psychiatric team. Tompkins³⁵ notes that of all personnel the nurse is best fitted to combat apathy and establish meaningful relations with patients whose recovery correlates with the amount of attention they receive. Two timely articles discuss why the psychiatric nurse fails to realize her full capacities. Weiner³⁶ makes good use of Reider's paper on human needs and nursing (referred to last year) to show how better education and training can raise professional status. In another paper, Devereux and Weiner¹³ explain how the nurse can provide the patients with the emotional gratifications and narcissistic supplies which are her real contribution. Clark⁹ reports on the various duties of directors of psychiatric nursing observed on her trip as nursing consultant of the American Psychiatric Association.

In two recent publications, the reviewers, together with Hargrove,^{8, 8a} discussing psychiatric treatment in general hospitals, stress the gap to be filled in training programs. Less than 300 of the total 4761 United States general hospitals train any psychiatric personnel. However, as Michael Reese in Chicago²⁷ and St. Francis in Pittsburgh¹ have demonstrated, general hospitals can greatly increase their training programs.

The psychiatric aspects of hospital administration come in for comment. Baganz³ used the conference system to encourage 1400 employees in presenting problems, ventilating annoyances and accepting suggestions for various difficulties. The administrator, like the group psychotherapist, must keep all promises, indulge in no ridicule and respect suggestions. In this way, Baganz considers that personnel can find useful, acceptable outlets for their drives.

OCCUPATIONAL THERAPY

Personnel. Some effort is being made to perfect methods for proper selection of capable students. To date, tests such as the Minnesota Multiphasic, Cardall Practical Judgment and Purdue Pegboard have been used to measure emotional stability and capacity to deal imaginatively with problems in construction. However, the best predictor is still the freshman orientation course, in which the staff supervisor closely observes new students in the weekly recreation programs.⁶¹ More study is needed regarding this important topic.

Problems of Research. Attention to research problems is another development of the past year. Goodrich et al.⁴⁸ in Boston Psychopathic hospital during a 6-month test period measured 45 psychotic patients' responses to varying approaches. Except for manic patients, all patients who improved

showed a definite increase in total activity, while the amount of random behavior decreased early. The trend toward socialization was more marked in manic depressive patients. These definite observations made the occupational therapist a more integral part of the psychotherapeutic team.

Hyde⁴⁰ studied social relations and creativity. One series of tests, approximating life situations, evaluated ego strength in a group of lobotomized patients. Other tests measured ability to recognize and fulfill social expectations, to shift tasks and to make object cathexes. A test series is being devised to predict higher levels of interpersonal relationships.

An interesting study by Macdonald and Lewis⁴³ comprised groups of elderly male and female patients, selected because of severe deterioration, in some cases amounting to stupor or mutism. Patient, persistent effort was used over a 6-month period. After careful comparisons, simple games such as country dancing and playing with bean bags proved more useful than crafts and arts. The authors give much practical information on handling seriously deteriorated patients.

Integration with Rehabilitation. The attempt to integrate occupational therapy with rehabilitation may mean less emphasis on avocations, as Wilson⁴³ points out. He advises beginning pre-industrial tryouts while mental patients are still in the hospital, thus enabling them to take advantage of important benefits of public law 113, passed in 1943. Garrett⁴⁷ explains how careful motivation aids the patient's rehabilitation. Cohen⁴¹ discusses vocational problems in such specific psychiatric disabilities as post-traumatic reaction, alcoholism, psychoses and injuries such as blindness. In these cases, the occupational therapist must cooperate with vocational and personnel counselors. Bozeman³⁹ studied vocational service as an adjunct to psychotherapy in 450 neurotics seen in 6 clinics; in three-fourths of those over age 45 no aid could be noted, while in 125 patients under age 30 the main problem concerned vocational maladjustment. This preliminary study requires closer, longer observation, for worthwhile results. Eventually, occupational therapy may be able to devise ways to prevent emotional and industrial maladjustment.

Therapy. An excellent article by Chambers⁴⁰ points out that the real concept of the neuropsychiatric team is not yet realized. Under supervision of a competent psychiatrist any team member may temporarily assume the dominant treatment role. In Chambers' opinion the increasing emphasis on psychiatric education means that occupational therapists and other auxiliary workers will have to keep pace by frequent, well planned graduate study and research.

Hardgrove⁴⁹ emphasizes the duties of the public health nurse and occupational therapist in studying problems of the chronically ill in the 500-bed research center of the National Institute of Health. Fraenkel⁴⁶ found both

directive and nondirective approaches effective in establishing rapport and getting the patient to participate in occupational therapy. Monroe⁵⁵ shows how occupational therapy can induce old people to study or to work at hobbies, thereby motivating new interests.

James⁵¹ details instructions for use of occupational therapy in training from very early years spastic, athetoid and ataxic types of cerebral palsy patients. The use of skill chart tests devised at Phelps Rehabilitation Institute is explained. Teamwork among all therapists is stressed, with the over-all purpose of enabling patients either to earn a living or, at least, to become more independent. Another excellent article is that of Rabinovitch et al.,⁵⁷ who successfully integrated recreational with occupational therapy in handling 28 children, aged 6 to 13, on a psychiatric ward. Practical ways of directing and consolidating the child's constructive interests are described. Even disturbed, destructive children are allowed to use tools under close supervision. For example, a girl of 12 was extremely hostile and refused to wear girl's clothes. At age 10 she had seen her psychotic father committed to a state hospital; her mother was frequently in and out of court on charges of sexual delinquency. After many stormy sessions, the girl's interests were aroused and directed first into jewelry designing, then into interior decorating. Treatment is thus able to give these disturbed children opportunities for patterned activities, impulse control, mastery of new skills and creative work. Stavisky's⁵⁹ interesting article describes the pioneering work with 170 criminally insane sexual psychopaths in Howard Hall, at St. Elizabeths. In this section, now directed by Cruvant and Abrahams, one ward was turned into a well equipped occupational therapy suite and for the first time a woman therapist was installed. Multiple activities are used in the effort to resocialize these patients.

Music continues to be discussed as therapy. A thoughtful editorial⁴⁵ notes such defects in many previous projects as poor planning, fragmentary observations, poorly presented results. Preston⁵⁶ finds the musician with a teaching background more helpful than the artist type. Both he and the Leedys⁶² attempt to differentiate the kind of music best suited to electroshock therapy. Of great value is the straight musical instruction provided in 114 VA hospitals by the Hospitalized Veterans Music Service, which gives some 4000 veterans instruction and uses nearly 30,000 in ward participation programs.⁴⁴

Stetson⁶⁰ reports efficient service of volunteers in occupational therapy in Boston Psychopathic Hospital. Ridgway's⁵⁸ suggestion is practical: since the volunteer program demands too much of the occupational therapist's time, a nonprofessional competent person should be trained to select, orient and instruct these workers.

An extremely useful article by West and Clark⁶² gives detailed plans for

adequate occupational therapy services suited to both smaller and larger hospitals. Floor plans and itemized lists of equipment and supplies, with suggested modifications, are included in this authoritative syllabus.

Recent publications include discussion of simple, inexpensive crafts;⁴³ and a timely reference list on crafts, teaching procedures, purchasing and other practical aspects.⁴²

Recently, Karl Menninger⁵⁴ noted the fact that occupational, recreational and other such adjunctive therapies cannot be carried on in Saskatchewan except in the presence of a trade unionist at full scale pay. This severely handicapping measure, enacted by the Labor Party, contrasts with the province's excellent system of training nurses and aides in psychiatric hospitals, which are now amply staffed with well trained, well paid personnel.

REFERENCES

Psychiatric Nursing

- ¹ Adele, S. M.: Care of mentally ill in general hospital. *Hospitals*. 25:53, 1951.
- ² Aushman, R.: Nurse as member of cerebral palsy team. *Nursing World*. 126:284, 1951.
- ³ Baganz, C. N.: Psychiatric aspects of hospital administration. *Am. J. Psychiat.* 108:277, 1951.
- ⁴ Bakwin, H.: Psychologic implications of early child care. *Am. J. Nursing*. 51:7, 1951.
- ⁵ Barron, E. M. and Donohue, H. H.: Psychiatric aide selection by psychological examination. *Am. J. Psychiat.* 107:859, 1951.
- ⁶ Bellam, G.: Tonsillectomy without fear. *Am. J. Nursing*. 51:244, 1951.
- ⁷ Bennett, A. E. and Eaton, J. T.: Role of psychiatric nurse in newer therapies. *Am. J. Psychiat.* 108:167, 1951.
- ⁸ Bennett, A. E., Hargrove, E. A., and Engle, B.: Present status of psychiatric facilities in general hospitals. *Am. J. Psychiat.* 108:321, 1951.
- ^{8a} —: Psychiatric treatment in general hospitals. *J. A. M. A.* 147:1019, 1951.
- ⁹ Clark, D. E.: Role of director of nursing—psychiatric. *Am. J. Psychiat.* 108:364, 1951.
- ¹⁰ Cooley, C. H.: *Social Aspects of Illness*. Philadelphia, W. B. Saunders, 1951.
- ¹¹ Cunningham, B. V.: *Psychology for Nurses*. 2nd edit. New York, Appleton-Century-Crofts, 1951.
- ¹² Davis, I. J.: *Handbook for Volunteers in Mental Hospitals*. Minneapolis, Univ. of Minnesota Press, 1951.
- ¹³ Devereux, G. and Weiner, F. R.: Occupational status of nurses. *Am. Sociolog. Rev.* 15:628, 1950.
- ¹⁴ Dix, A. A.: Modern psychiatric nursing. *Am. J. Psychiat.* 107:695, 1951.
- ¹⁵ Farnsworth, D. L.: Nurse's role in mental health. *Pub. Health Nursing*. 43:173, 1951.
- ¹⁶ Fechner, A. H. and Parke, J. H.: Volunteer worker and psychiatric hospital. *Am. J. Psychiat.* 107:602, 1951.
- ¹⁷ Fine, B.: Nursing education put up to colleges. *New York Times*, June 4, 1951.

- ¹⁸ Freeman, L.: Mental hospital trains technicians. *New York Times*, Dec. 6, 1951.
- ¹⁹ Gayle, R. F.: Role of general hospital in care of mentally ill. *Am. J. Psychiat.* 108:103, 1951.
- ²⁰ Greiling, G. E.: Myasthenia gravis and nursing care. *Am. J. Nursing.* 51:655, 1951.
- ²¹ Haddock, J. N. and Dundon, H. D.: Volunteer work in state hospital. *Ment. Hyg.* 35:599, 1951.
- ²² Jeffers, F. C.: Preparation for marriage. *Am. J. Nursing.* 51:514, 1951.
- ²³ Kaldeck, R.: Group psychotherapy by nurses and attendants. *Dis. Nerv. System.* 12:138, 1951.
- ²⁴ Kremsdorf, D.: Redefining role of psychiatric nurse. *Nursing World.* 125:109, 1951.
- ²⁵ Matheney, R. V.: How does psychiatric nursing affiliation fail? *Am. J. Nursing.* 51:684, 1951.
- ²⁶ Mereness, D.: Preparation of nurse for psychiatric team. *Am. J. Nursing.* 51:320, 1951.
- ²⁷ Michael Reese opens psychiatric institute. *Hosp. Management* 71:47, 1951.
- ²⁸ Nace, F. D.: Care of aged in state mental hospital. *Am. J. Nursing.* 51:366, 1951.
- ²⁹ National League of Nursing Education: Report on advanced programs in psychiatric nursing. 1951.
- ³⁰ Newton, K.: *Geriatric Nursing*. St. Louis, C. V. Mosby, 1950.
- ³¹ Pescor, M. J. and Walker, P. K.: Treatment of drug addiction. *Am. J. Nursing.* 51:611, 1951.
- ³² Smith, M.: Preparing student for psychiatric affiliation. *Am. J. Nursing.* 51:47, 1951.
- ³³ Stetson, H. C.: A mental hospital enlists voluntary worker. *Hospitals.* 25:54, 1951.
- ³⁴ Stevens, L. F.: Care of psychologic casualties in atomic disaster. *Am. J. Nursing.* 51:513, 1951.
- ³⁵ Tompkins, H. and Ozarin, L. D.: Changing concepts of role of institutional psychiatrist. *Psychiatric Quart. Suppl.* 24:23, 1950.
- ³⁶ Weiner, F. R.: Professional consequences of nurse's occupational status. *Am. J. Nursing.* 51:614, 1951.
- ³⁷ Yerbury, E. C., Holzberg, J. D., and Alessi, J. L.: Psychological tests in selection of psychiatric aides. *Am. J. Psychiat.* 108:91, 1951.
- ³⁸ Zeman, F. D.: Professional nurse in care of aged. *J. Gerontol.* 6:146, 1951.

Occupational Therapy

- ³⁹ Bozeman, M. F.: Vocational services as adjunct to psychotherapy. *Ment. Hyg.* 35:212, 1951.
- ⁴⁰ Chambers, R. E.: Recent developments in field of psychiatry. *Am. J. Occup. Therapy.* 5:97, 1951.
- ⁴¹ Cohen, N.: Role of psychiatrist in rehabilitation of disabled veteran. *Dis. Nerv. System.* 12:3, 1951.
- ⁴² Colorado Occupational Therapy Association: *At Your Fingertips*. 1950.
- ⁴³ Cox, D. and Warren, B.: *Creative Hands*. New York, John Wiley, 1951.
- ⁴⁴ Editorial: Music for veterans. *New York Times.* 101:26, Dec. 7, 1951.
- ⁴⁵ Editorial: Musicians' claim to treatment. *Am. J. Psychotherapy.* 5:495, 1951.
- ⁴⁶ Fraenkel, W. L.: Establishing rapport. *Am. J. Occup. Therapy.* 5:194, 1951.
- ⁴⁷ Garrett, J. F. and Myers, J. S.: Motivation and rehabilitation. *Occup. Therapy.* 30:296, 1951.

- ⁴⁸ Goodrich, D. W., Bockhoven, J. S., and Hyde, R. W.: Behavioral characteristics of recovery from psychosis. *Occup. Therapy.* 30:147, 1951.
- ⁴⁹ Hardgrove, T. J.: Problems of chronically ill. *Am. J. Occup. Therapy.* 5:9, 1951.
- ⁵⁰ Hyde, R. W.: Occupational therapy research laboratory. *Occup. Therapy.* 30:133, 1951.
- ⁵¹ James, E. M.: Occupational therapy for cerebral palsy. *Brit. J. Phys. Med.* 14:149, 1951.
- ⁵² Leedy, J. and Leedy, D.: Use of music with electro-convulsive therapy. *Dis. Nerv. System.* 12:281, 1951.
- ⁵³ Macdonald, J. M. and Lewis, H. M.: Occupational therapy in mental hospital. *Edinburgh M. J.* 58:336, 1951.
- ⁵⁴ Menninger, K. A.: Personal communication.
- ⁵⁵ Monroe, R. T.: A new medical look at old age. *Am. J. Occup. Therapy.* 5:12, 1951.
- ⁵⁶ Preston, M. J.: Organization of music program as rehabilitation for mentally ill. *Psychiatric Quart. Suppl.* 24:119, 1950.
- ⁵⁷ Rabinovitch, R. D., Bee, J., and Outwater, B.: Integration of therapies in psychiatric treatment of children. *Am. J. Occup. Therapy.* 5:1, 1951.
- ⁵⁸ Ridgway, E. R.: Volunteer program at Delaware State Hospital. *Am. J. Occup. Therapy.* 5:205, 1951.
- ⁵⁹ Stavisky, S.: Mental hospital with a heart. *Hosp. Management.* 71:46, 1951.
- ⁶⁰ Stetson, E. R.: Role played by volunteers in mental hospital. *Am. J. Occup. Therapy.* 5:203, 1951.
- ⁶¹ Thompson, C. G.: Preliminary notes on selecting students for occupational therapy. *Am. J. Occup. Therapy.* 5:191, 1951.
- ⁶² West, W. L. and Clark, A. W.: Planning the complete occupational therapy service. *Hospitals.* 25:85, 1951.
- ⁶³ Wilson, S. C.: Integration of occupational and recreational therapy. *Am. J. Occup. Therapy.* 5:198, 1951.

Rehabilitation

By MORTON MARKS, M.D. AND LEE B. GREENE, M.D.

THE present concept of rehabilitation has become a dynamic one and its values and basic philosophy are being appreciated and applied with increasing frequency in the field of neurology and psychiatry.

Rusk^{77, 81} considers chronic diseases in an aging population medicine's number one problem. Temple⁸⁶ stresses that rehabilitation is a medical problem and a unified process, in which medical and surgical treatments are stages. Bingham⁹ identifies psychosomatic medicine with rehabilitation, and stresses the application of its principles in therapy. Holland⁵⁰ considers it to be one of the most far-reaching advances accomplished during the war and the years immediately after. Gingras and Mongeau³⁹ recognize the values and need for rehabilitation in many of the common chronic illnesses, including cerebral palsy, multiple sclerosis, hemiplegia and paraplegia. They correctly deplore the lapse of time ensuing between active treatment and the utilization of rehabilitation technics. Bailey⁴ reviews the philosophy, principles and historic background of the modern rehabilitation movement. Its special application in the field of neurology is comprehensively discussed.

The magnitude of the problem is attested to by Covalt²⁰ in that more than 25 per cent of her case load were neurologic problems. She emphasizes that age alone is not the determining factor, but rather that there must be an adequate time allotment of at least three months for a comprehensive training program.

Piersol⁶⁶ stresses the *role the physiatrist* will be expected to assume in order to meet the broad rehabilitation program anticipated by our aging population. The educational problems associated with this are discussed by Rusk.⁷⁸

The *importance of teamwork* has repeatedly been emphasized^{32, 55, 56, 83, 89}. The roles of the *clinical psychologist*,³² *occupational therapist*^{17, 40} and *corrective therapist*,¹⁰⁰ have been examined. The importance of *physical therapy* in rehabilitation is stressed by Raus.⁷³ Smith⁸⁴ reviews the value of physical therapy in the care of psychiatric patients and lists the different modalities useful in their management.

Pentreath⁶⁵ outlines a broad program for the *rehabilitation of psychiatric patients* and considers the emotional attitudes of the patient once he is hospitalized. The role of the *psychiatrist* in the rehabilitation of the disabled veteran is examined by Cohen.¹⁸ He reviews the symptoms and treatment of a number of conditions, including post-traumatic reactions, alcoholism, epilepsy, psychotics and mental defectives. The *psychologic impact of physical disability* is discussed by Rusk.⁷⁹

In studying the *psychiatric aspects* of rehabilitation, Grayson^{42, 43} concludes that rehabilitation requires an understanding of the total patient, that workers in rehabilitation must be aware of their own attitudes toward disability and objective in dealing with emotional problems. He feels that "acceptance" is the core of functional rehabilitation and involves psychobiologic incorporation and social integration. He emphasizes that psychologically this consists essentially of a fortification of the defenses the patient is struggling with and that the psychiatric team functions directly by psychotherapy and indirectly by education of other workers as to the individual psychologic needs of the patient. Garrett and Myers³³ discuss the *problems of motivating disabled persons*, their frequent non-acceptance of their disability and the utilization of it as a neurotic defense. They feel it is important for the patient to be aware of his emotional reaction to his disability. The importance of *psychosocial and spiritual factors* in rehabilitation is stressed by Morrissey.⁶¹

Levi⁵⁸ in attempting to correlate *Rorschach patterns* with personality structure in predicting the success of a rehabilitation program finds that patients with a high percentage of anatomy responses made minimal progress in rehabilitation. Those in whom a neurotic personality structure was portrayed (by a high percentage of F+ responses and aggressive animals) showed the maximum progress.

The important contribution that *vocational training* has to offer is emphasized by Whitehouse.⁹⁴ In an interesting article Bozeman¹² concludes from a study of 450 neurotic patients that emotional vocational problems are best met when psychiatric, educational and vocational services have common goals. The problems of the handicapped student received the attention of Condon¹⁹ and Hardee.⁴⁴ Di Michael²⁷ discussed the vocational rehabilitation of the mentally retarded and sets forth a specific program. Kratz⁵⁷ recounted the major developments in the evolution of federal legislation for the vocational rehabilitation of the civilian disabled.

Wiles⁹⁵ stresses the importance of *industrial rehabilitation* as complementary to medical rehabilitation. Breuil¹³ believes that adequate rehabilitation requires the cooperation of industry and labor unions. The operation of the Goodwill Industries is described by Zelle,¹⁰¹ and considered as a

rehabilitative sheltered workshop. He demonstrates how the counselor can efficiently utilize their resources.

Minski⁶⁰ believes that the individual must be considered a part of the community and his social problems and difficulties must be studied from many angles for a satisfactory adjustment. Thomas⁸⁷ defines *resocialization* as a restoration of a normal attitude to self and society, and considers it equally as important as the restoration of physical fitness.

Afanasev¹ reports benefits from a physical exercise program given to a series of *catatonic schizophrenics*. Burlingame¹⁵ prior to his death, was firmly convinced of the importance of rehabilitation as an *ancillary to psycho-surgery*. He cautioned against prematurely overloading the newly convalescent patient with emotional stresses and advocated the use of the sheltered workshop. Winnik and Askenazy⁹⁷ emphasize that the postoperative milieu is so important that such factors as the social setting and working conditions to which the patient may return should be evaluated before lobotomy is to be performed. Rackow and McGriff⁷¹ outline their comprehensive program used to rehabilitate the *prefrontal lobotomy patient*. They include a valuable list of instructions furnished to guardians at the time the patient leaves the hospital.

From experience gained in rehabilitating the *crippled child*, Gillette³⁶ emphasizes that he needs a means of communication, ability to care for himself, education, security, love and recognition and the ability to walk. The emotional problems of children with physical disabilities differs from that of the normal¹⁰² and it is recognized that the development and function of a child's personality may be affected by prolonged invalidism.²⁵ Hipps⁴⁷ offers suggestions in attempting training of the "hopeless" *cerebral palsy* patient and he stresses always keeping the child's activities and problems within the stage of maturation he has obtained.

The problem of retraining the *brain injured patient* is considered by Brown.¹⁴ Rankin⁷² describes the treatment of the *cerebrovascular accident*, emphasizing that the program must be started early in the acute phase. There are many, however, who will disagree with his theoretic neurophysiologic formulations. The problems and details of the rehabilitation of the *hemiplegic* has again been extensively reviewed.^{6, 16, 21, 31, 35, 67, 75, 76, 90, 99} Van Buskirk and Zarling⁸⁸ utilized the EEG as a prognostic guide in the rehabilitation of the vascular hemiplegic and found that the more severe the EEG abnormality, the longer the stay in the hospital and the greater the residual disability.

Wépman's⁹² volume based on his vast first-hand experience with *aphasia* is a significant contribution, although some of his theoretic considerations are controversial. It is stimulating in that his approach is one of attaining

various successive gestalt levels, in contrast to the relatively ineffectual phonetic one commonly used.

It is a measure of a specialty's maturity when it seeks scientific validation of the efficacy of its methods. Such an approach has been made by Rinzier, Brown and Benton^{7, 74} in evaluating physical and drug therapy in the rehabilitation of the hemiplegic patient. From their data the value of a comprehensive program is unquestioned.

In view of the fact that hemiplegia is a frequent concomitant of cardiac disease, the experimental work of Benton, Brown and Rusk⁸ in determining the energy expenditure required in performing the activities necessary for daily living, is significant.

The rehabilitation program and problems of the *paraplegic*,^{11, 26, 28, 30, 37, 38, 48, 49, 59, 62, 68, 70, 82, 85, 91} the *patient with polio*,^{22, 23, 45, 80} *multiple sclerosis*^{5, 24, 41, 93} and *peripheral nerve injuries*³⁴ have been described.

Gordon's⁴¹ manual should prove a useful guide in the management of all chronic disabilities, not only *multiple sclerosis*, as will Morrissey's⁶³ detailed text on *rehabilitation nursing*. Newman and Jameson⁶⁴ discuss assistive devices for the disabled, and an extensive compilation, excluding braces and prosthesis, with photographs, sources and costs, has been made available.¹⁰⁴

The appreciation of the need for rehabilitation is worldwide. There are pleas for and evaluations of their assets and programs from Austria,²⁹ Argentina,² Czechoslovakia,^{51, 54, 69} Finland,⁵² France,¹⁰³ Great Britain,⁴⁶ Ireland,³ Germany,¹⁰ South Africa⁹⁸ and the USSR.⁵³ Unfortunately, most of the emphasis has been on the physical disability with insufficient attention to the psychiatric aspects of the problem and in many instances with the complete exclusion of psychiatric patients. The United Nations coordinated program for the social rehabilitation of the physically handicapped is described by Wilson.⁹⁶ He lists the *international organizations* interested in the problem.

REFERENCES

- ¹ Afanasev, I. N.: Experiments with physical exercises for inhibited and agitated catatonics. *Nevropat. i psikhiat.* 19:38, 1950.
- ² Anibaldi, N.: La rehabilitacion de los traumatizados. *Prensa méd. argent.* 36: 2658, 1950.
- ³ Atkins, R. G.: Physical medicine: rehabilitation. *Med. A. Eire.* 27:102, 1950.
- ⁴ Bailey, P.: Neurologic rehabilitation. *Neurology.* 1:475, 1951.
- ⁵ Baker, A. B.: Multiple sclerosis—Its diagnosis and treatment. *Wisconsin. M. J.*
- ⁶ Benton, J. G. and Rusk, H. A.: Rehabilitation and cardiovascular disease. *Mod. Concepts Cardiovas. Dis.* 19:85, 1950.
- ⁷ Benton, J. G., Brown, H., and Rinzier, S. H.: Objective evaluation of physical and drug therapy in the rehabilitation of the hemiplegic patient. A study of dihydroergocornine (DHO-180). *Am. Heart J.* 42:719, 1951.

- ⁸ Benton, J. G., Brown, H., and Rusk, H. A.: Energy expended by patients on the bedpan and bedside commode. *J. A. M. A.* 144:1443, 1950.
- ⁹ Bingham, C. T.: Psychosomatic medicine and rehabilitation. *Connecticut M. J.* 14: 725, 1950.
- ¹⁰ Boni, A.: Die eingliederung von rekonvaleszenten und chronisch kranken in der arbeitprozess. *Veska Zeitschr.* 13:401, 1949.
- ¹¹ Bors, E.: Urological aspect of rehabilitation in spinal cord injuries. *J. A. M. A.* 146:225, 1951.
- ¹² Bozeman, M. F.: Vocational services as an adjunct to psychotherapy. *Ment. Hyg.* 35:212-220, 1951.
- ¹³ Breuil, G.: Un centre de deadaptation et de reeducation. *Tech. Hosp.* 5:47, 1950.
- ¹⁴ Brown, J. R.: Retraining patients with brain damage. *Lancet.* 70:455, 1950.
- ¹⁵ Burlingame, C. C.: An important ancillary of psychosurgery. *An. portug. psiq.* 2:11, 1951.
- ¹⁶ Burnham, C. R.: Physical medicine and rehabilitation for patients with hemiplegia. *J. Maine M. A.* 42:173, 1951.
- ¹⁷ Clarke, M. D.: Occupational therapy's part in the rehabilitation of the chronic neurological patient. *Mil. Surgeon.* 108:331, 1951.
- ¹⁸ Cohen, N.: Role of psychiatrist in the rehabilitation of the disabled veteran. *Dis. Nerv. System.* 12:3, 1951.
- ¹⁹ Condon, M. E.: Helping the handicapped student. *J. Rehabilitation.* 17:14, 1951.
- ²⁰ Covalt, N. K.: Physical medicine and rehabilitation study. One year report in particular relation to the chronically ill. *J. A. M. A.* 144:1249, 1950.
- ²¹ Deaver, G. G.: The rehabilitation of the hemiplegic. *Rhode Island M. J.* 34:421, 1951.
- ²² —: Rehabilitation of poliomyelitis patients. *Postgrad. Med.* 9:155, 1951.
- ²³ —: A study of the adjustment of 500 persons over 16 years of age with disabilities resulting from polio. *New York Med.* 7:16, 1951.
- ²⁴ —: Physical therapy and rehabilitation in multiple sclerosis. *Crippled Child.* 30:11, 1950.
- ²⁵ De La Fuente, R. and Torres, L.: Problemas emocionales del nino lisiado. *Bol. méd. Hosp. Inf.* 7:194, 1950.
- ²⁶ Denning, K. A., Deyoe, F. S., and Ellison, A. B.: Ambulation: Physical Rehabilitation for Crutch Walkers. New York, Funk & Wagnalls Co., 1951, pp. 188.
- ²⁷ Di Michael, S. G.: Vocational Rehabilitation of the Mentally Retarded. Washington, D. C., Fed. Sec. Agency, Off. Voc. Rehab., 1950.
- ²⁸ Dinken, H.: Physical treatment and rehabilitation of the paraplegic patient. *J. A. M. A.* 146:232, 1951.
- ²⁹ Erlacher, P. J.: Problems of rehabilitation in Austria. *Occup. Therapy*, 29:354, 1950.
- ³⁰ French, J. D.: Neurosurgery in the rehabilitation of paraplegics. *J. A. M. A.* 146:223, 1951.
- ³¹ Gamble, S. G. and Zeiter, W. J.: Physical therapeutic measures in hemiplegia. *Cleveland Clin. Quart.* 18:217, 1951.
- ³² Garrett, J. F. and Myers, J. S.: Clinical psychology in the rehabilitation process. *J. Rehab.* 17:3, 1951.
- ³³ —: Motivation and rehabilitation. *Occup. Therapy.* 30:296, 1951.
- ³⁴ Ghiora, A.: Rehabilitation of peripheral nerve injuries. *Harefuah.* 40:79, 1951.
- ³⁵ — and Adler, E.: Tonus modifying and mass reflexes in the rehabilitation of hemiplegics. *Occup. Therapy.* 30:217, 1951.

- ³⁶ Gillette, H. E.: Rehabilitation of the crippled child. *J. M. A. Georgia*. 39:332, 1950.
- ³⁷ Gingras, G.: Rehabilitation of civilian paraplegics in Canadian department of veteran's affairs hospitals. *Arch. Phys. Med.* 31:772, 1950.
- ³⁸ —: Rehabilitation of the paraplegic. *Treat. Serv. Bull.* 5:481, 1950.
- ³⁹ — and Mongeau, M.: *Médecine physique et réhabilitation*. Union méd. du Canada. 79:873, 1950.
- ⁴⁰ Goodrich, D. W., Bockoven, J. S., and Hyde, R. W.: Behavioral characteristics of recovery from a psychosis. *Occup. Therapy.* 30:147, 1951.
- ⁴¹ Gordon, E. E.: *Multiple Sclerosis: Application of Rehabilitative Techniques*. New York, National Multiple Sclerosis Monograph, 1951.
- ⁴² Grayson, M.: Psychiatric aspects of rehabilitation. *Arch. Neurol. & Psychiat.* 64:899, 1950.
- ⁴³ —: Concept of "acceptance" in physical rehabilitation. *J. A. M. A.* 145:893, 1951.
- ⁴⁴ Hardee, M. D.: When your client goes to college. *J. Rehab.* 17:10, 1951.
- ⁴⁵ Hauser, E. D. W.: Planning for home-care treatment. *Hospitals.* 25:47, 1951.
- ⁴⁶ Hendelberg, Th.: A review of rehabilitation programs in England during the summer of 1949. *Soc. med. tskr.* 27:89, 1950.
- ⁴⁷ Hipps, H. E.: Teaching training principles for the "hopeless" cerebral palsy patient. *Phys. Therapy Review.* 31:180, 1951.
- ⁴⁸ Hoberman, M. and Cicienia, E. F.: Rehabilitation techniques with braces and crutches I. *Occup. Therapy* 30:203, 1951.
- ⁴⁹ —: Rehabilitation techniques with braces and crutches II. *Occup. Therapy.* 30:282, 1951.
- ⁵⁰ Holland, T. E.: Rehabilitation of the disabled. *Manitoba M. Rev.* 30:637, 1950.
- ⁵¹ Hulek, A.: Rehabilitation of the physically handicapped in Czechoslovakia. *Polski tygodnik. lek.* 5:186, 1950.
- ⁵² Jansson, K.: Rehabilitation of Finland's disabled. *J. Rehab.* 17:10, 1951.
- ⁵³ Jazykov: Treatment of the disabled in the U. S. S. R. *Acta chir. orthop et traumatol. čechoslov.* 17:2, 1950.
- ⁵⁴ Karpin, B. and Obrda, K.: Rehabilitation. *Českoslov. Nemocnice.* 17:297, 1949.
- ⁵⁵ Kern, R. A.: Improvement of professional relations in hospitals. *Dept. Med. Surg. Inf. Bull.* IB 10-17:3, 1951.
- ⁵⁶ Kessler, H.: Recent achievements in rehabilitation. *Rehabilitation.* 1:8, 1951.
- ⁵⁷ Kratz, J. A.: How federal laws made vocational rehabilitation history. *J. Rehabilitation.* 17:16, 1951.
- ⁵⁸ Levi, J.: Rorschach patterns predicting success or failure in the rehabilitation of the physically handicapped. *J. Abnorm. & Social Psychol.* 46:240, 1951.
- ⁵⁹ Manson, M. P.: Motivations in the rehabilitation of paraplegics. *Arch. Neurol. & Psychiat.* 65:34, 1951.
- ⁶⁰ Minski, L.: Some recent advances in the rehabilitation of the psychoneurotic patient. *M. Press.* 225: 12, 1951.
- ⁶¹ Morrissey, A. B.: Psychosocial and spiritual factors in rehabilitation. *Am. J. Nursing.* 50:12, 1950.
- ⁶² —: The procedures of urinary and bowel rehabilitation. *Am. J. Nursing.* 51: 194, 1951.
- ⁶³ —: *Rehabilitation Nursing*. New York, G. P. Putnam & Sons, 1951, pp. 296.
- ⁶⁴ Newman, L. B. and Jameson, E. L.: Assistive devices for the disabled. *Occup. Therapy.* 30:8, 1951.

- ⁶⁵ Pentreath, E. U. H.: Some methods in the rehabilitation of psychiatric patients. M. Press. 226:426, 1951.
- ⁶⁶ Piersol, G. M.: The present obligation of physical medicine and rehabilitation. J. A. M. A. 147:1093, 1951.
- ⁶⁷ Pincook, J. G.: Management of hemiplegics. Manitoba M. Rev. 30:75, 1951.
- ⁶⁸ Pique, J. A. and Lucero, N.: El uso de bastones y muletas en la reeducacion de la marcha. Dia méd. 22:2616, 1950.
- ⁶⁹ Polakova, Z.: Rehabilitation camp for physically handicapped children at Svojsice near Prague. Acta chir. orthop et traumatol. Čecoslov. 17:96, 1950.
- ⁷⁰ Pollock, L. J., Arieff, A. J., Newman, L. B., and Kesert, B. H.: Management of residuals of injuries to spinal cord and cauda equina. J. A. M. A. 146:1551, 1951.
- ⁷¹ Rackow, L. L. and McGriff, D. L.: Rehabilitation of the prefrontal lobotomy patient. Occup. Therapy. 29:329, 1950.
- ⁷² Rankin, R. M.: Treatment of cerebrovascular accident. Phys. Therapy Rev. 31:81, 1951.
- ⁷³ Raus, G. M.: The role of physical therapy in rehabilitation. New York State J. Med. 51:509, 1951.
- ⁷⁴ Rinzler, S. H., Brown, H., and Benton, J. G.: A method for the objective evaluation of physical and drug therapy in the rehabilitation of the hemiplegic patient. Am. Heart. J. 42:710, 1951.
- ⁷⁵ Rottjer, E. H.: Rehabilitation of the hemiplegic. Prensa méd. argent. 38:1946, 1951.
- ⁷⁶ Rudin, L., Levine, L., Hayes, E. R., and Cronin, D. J.: Rehabilitation of the hemiplegic with orthopedic disabilities. Occup. Therapy. 30:14, 1951.
- ⁷⁷ Rusk, H. A.: The internist's number one problem: Chronic disease in an aging population. Ann. Int. Med. 33:1341, 1950.
- ⁷⁸ —: Physical medicine and rehabilitation: The problems of education. Arch. Phys. Med. 32:3, 1951.
- ⁷⁹ —: The psychological impact of physical disability. Occup. Therapy. 13:4, 1950.
- ⁸⁰ —: Rehabilitation services for the polio patient. Hospitals. 25:49, 1951.
- ⁸¹ — and Taylor, E. J.: Rehabilitation. Ann. Am. Acad. Polit. & Social. Sc. 273:138, 1951.
- ⁸² Sanders, E. M.: Mobilization of paraplegics III. Crutch walking. Occup. Therapy. 30:61, 1951.
- ⁸³ Sensenich, H.: Team work in rehabilitation. Am. J. Pub. Health. 40:969, 1950.
- ⁸⁴ Smith, L. E.: Role of physical therapy in care of psychiatric patients. Phys. Therapy Rev. 31:126, 1951.
- ⁸⁵ Street, D. M.: Treatment and rehabilitation of paraplegics. Am. J. Surg. 80:722, 1950.
- ⁸⁶ Temple, A. D.: Rehabilitation as it concerns the physician. Treat. Serv. Bull. 5:475, 1950.
- ⁸⁷ Thomas, D. F.: An experiment in social rehabilitation. Brit. M. J. 1:404, 1951.
- ⁸⁸ Van Buskirk, C. and Zarling, V. R.: EEG prognosis in vascular hemiplegia rehabilitation. Arch. Neurol. & Psychiat. 65:732, 1951.
- ⁸⁹ Van Nostrand, F. H.: Rehabilitation of the neuropsychiatric patient. Treat. Serv. Bull. 5:496, 1950.
- ⁹⁰ von Wersowetz, O. F.: Supportive appliances for ambulatory rehabilitation of hemiplegics. Phys. Therapy. Rev. 31:13, 1951.

- ⁹¹ Wassen, W.: Guttman's method of transverse myelitis treatment. *Med. Klin.* 46: 30, 1951.
- ⁹² Wepman, J. M.: Recovery from Aphasia. New York. Ronald Press Co., 1951, pp. 276.
- ⁹³ Wertz, S. H.: Basic exercises in the treatment of multiple sclerosis and similar diseases of neuromuscular dysfunction. *J. A. Phys. & Ment. Rehab.* 4:16, 1951.
- ⁹⁴ Whitehouse, F. A.: Vocational training in a rehabilitation center. *J. Rehabilitation.* 17:3, 1951; 17:19, 1951.
- ⁹⁵ Wiles, H.: Rehabilitation from the industrial point of view. *Rehabilitation.* 1:3, 1951.
- ⁹⁶ Wilson, D. V.: Rehabilitation and the international service. *J. Rehabilitation,* 17:3, 1951.
- ⁹⁷ Winnik, Z. H. and Askenazy, H.: Our psychosurgical experiences. *Harefuah.* 39:19, 1950.
- ⁹⁸ Woolff, M. G.: Rehabilitation of the industrial worker. *South African M. J.* 24: 734, 1950.
- ⁹⁹ Yamshon, L. J.: Rehabilitation of the patient with hemiplegia. *California Med.* 73: 181, 1950.
- ¹⁰⁰ Yarosh, M.: Techniques in motivating acute neuropsychiatric patients via corrective therapy. *J. A. Phys. & Ment. Rehab.* 4:14, 1951.
- ¹⁰¹ Zelle, J. A.: Goodwill has found a good way. *J. Rehabilitation.* 17:3-17, 1951.
- ¹⁰² Erziehung als teil eines Gesamtplans fur das Koroerbehind. *Gesundh. Wohlf.* 30:433, 1950.
- ¹⁰³ Le reclassement professionnel des diminués physiques. Ministry of Labor and Social Security. *Med. Usine.* 12:236, 1950.
- ¹⁰⁴ Self-help Devices for Rehabilitation. New York University-Bellevue Med. Center Institute of Physical Medicine and Rehabilitation, New York.

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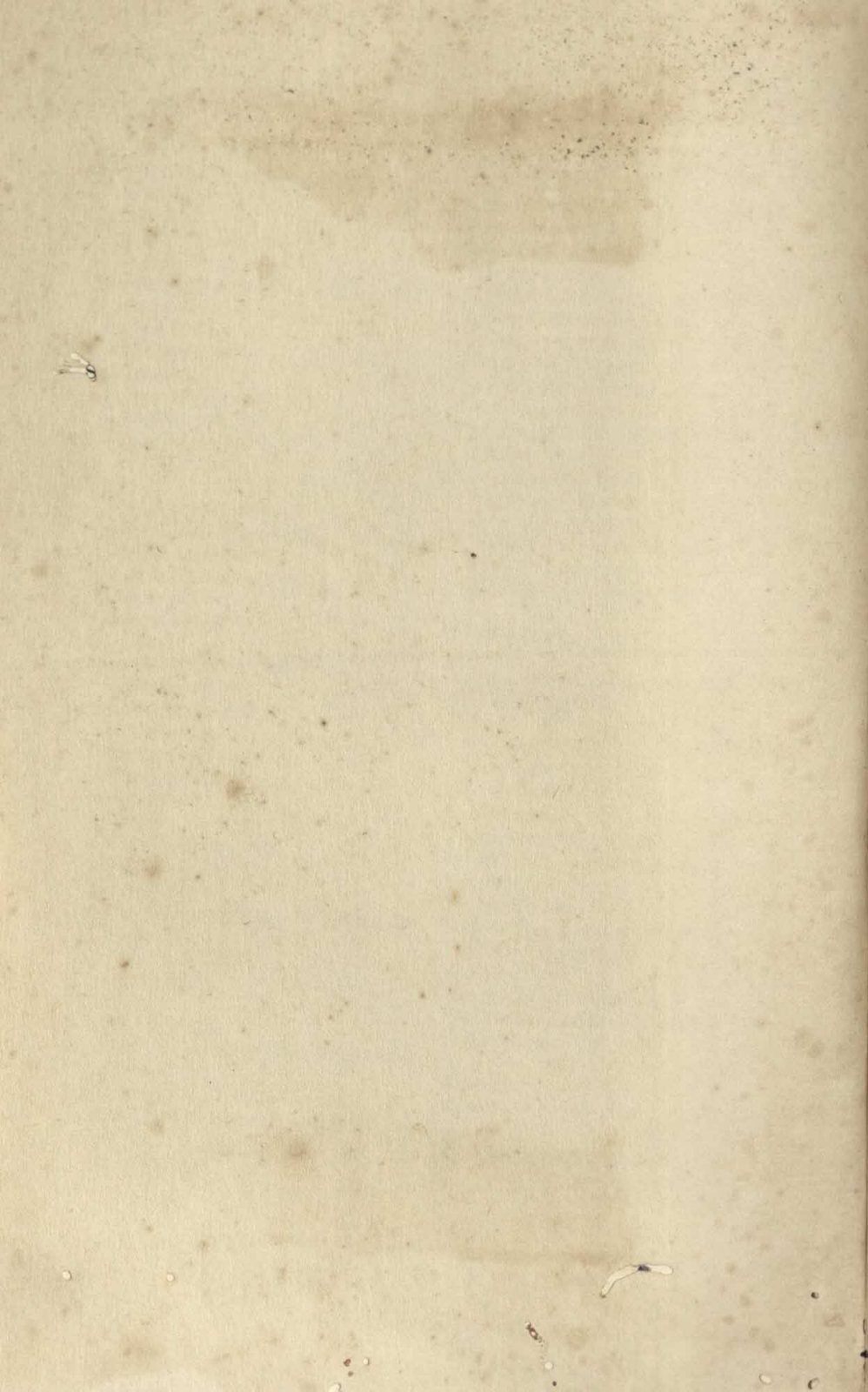
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